Your Health in good Hands
Germany takes a leading position in medicine.

German hospitals, clinics and medical doctors enjoy an excellent reputation. The continuously rising number of patients, who come to Germany to receive medical treatment and support, strongly confirms this fact.

Patients from the Gulf States gladly come to Germany to receive medical treatment because they regard Germany as a safe place and rely on German clinics and physicians. They feel welcome as guests and enjoy that they are encountered in an open-minded and friendly way.

German Medical Council, partner of renowned German hospitals, clinics and specialized practices, organizes the best medical treatment for patients from all over the world and offers them a full service package.

Германия занимает лидирующую позицию в области медицины.

Германская больницы, клиники и врачи имеют прекрасную репутацию. Постоянно растущее число иностранных пациентов, которые приезжают в Германию на лечение, подтверждает этот факт.

Пациенты со всего мира с удовольствием едут в Германию на лечение, поскольку рассматривают Германию как безопасную страну и доверяют немецким клиникам и врачам. Они чувствуют себя желанными гостями и наслаждаются местным гостеприимством.

Германский Медицинский Совет является партнером известных немецких клиник, медицинских центров, специалистов и организует самое лучшее лечение для пациентов со всего мира, предлагая им весь спектр услуг.
Limited Time Offer! Save $300 with code ZBY936, not applicable to government rates. To qualify, contact us at +1 781-936-2500 by June 30, 2010.

The World Health Care Congress Middle East

DECEMBER 5-7, 2010 • ABU DHABI, UAE

GLOBAL BEST PRACTICES TO DELIVER THE BEST HEALTH CARE

The World Health Care Congress Middle East is the most prestigious health care event, convening more than 500 global thought leaders and key decision-makers from all sectors of health care to share global best practices.

The 2010 event will feature top industry influencers, including health ministers, leading government officials, hospital directors, IT innovations and pharmacy and medical device companies.

The WORLD HEALTH CARE CONGRESS MIDDLE EAST WILL FEATURE EXECUTIVE SUMMITS ON:

- Hospital/Health Systems
- Chronic Care
- Health Technology and Interoperability
- Health Care Innovation and Investment
- Emerging Health Care Business Models
- Public and Population Health

For programming inquiries please contact us at: Programming@worldcongress.com

To register, please visit www.worldcongress.com/middleeast | Phone: +1 781-936-2500
Fax: +1 781-939-2543 | Email: wcreg@worldcongress.com
Dear Reader,

NEW: German Medical Journal now also in Russian-English and Spanish-English

The German Medical Journal will now be published in Russian-English and Spanish-English. This is our response to the incredibly high access rates of readers from the Russian Federation, the USA and the Spanish-speaking countries of Middle and South America to the Arabic-English version of the German Medical Journal. They represent the second- and third-largest group after the Arabic-speaking readers.

These two new editions certainly appeals to many other non-Arabic readers, who have so far been reading the journal the Arabic way «from back to front».

The two editions will lead to a significantly increased distribution of the German Medical Journal to regions which the German medicine is extremely interested in.

Brilliant and revolutionary: The iPad by Apple gets off to a rapid start worldwide.

On 28th May Apple has started the market launch of the iPad in Germany. As is already obvious, its success will be breathtaking. In the USA more than 300,000 iPads were sold already on the first day.

The new device will revolutionise the world of media: it will impart digital media an incredible boost. The iPad provides digital publications a clear advantage over printed media: they are available online with brilliant image quality. Anytime and anywhere.

German Medical Journal has seen this development coming and consistently focussed on digital distribution.

Enjoy your
German Medical Journal.

Nadine Baume
Managing Director
Current Standards in Diverticular Disease

Lung Cancer - Progress in Patient Care

Diagnosis and Treatment of Morbid Obesity

Modern Knee Arthroplasty

Predictive molecular testing and prevention of hereditary non-polyposis colorectal cancer syndrome (HNPCC, Lynch Syndrome)

Transcatheter Valve Therapies

Change of paradigm in dental local anesthesia: Alternatives to IANB and infiltration anesthesia

Improving the Care of Depressed Patients and Preventing Suicides - The European Alliance Against Depression
Стандарты диагностики и лечения дивертикулярной болезни

Рак легких: прогресс в лечении

Междисциплинарный подход в диагностике и лечении патологического ожирения

Современная артропластика коленного сустава

Предиктивное молекулярное тестирование и профилактика наследственного неполипозного колоректального рака (ННПКР, синдрома Линча)

Транскатетерная имплантация сердечных клапанов

Изменение парадигмы стоматологической местной анестезии - Альтернатива проводниковой и инфилтратционной анестезии

Улучшение помощи пациентам с депрессией и профилактика суицидальности - Европейский Альянс борьбы с депрессией
Russian Health Care Week

Expocentre Fairgrounds
Moscow, Russia

20th International Exhibition
for Health Care, Medical Engineering
and Pharmaceuticals

ZDRAVOOKHRANENIYE

6–10 December 2010

Organized by

EXPOCENTRE
INTERNATIONAL EXHIBITIONS AND CONVENTIONS
MOSCOW

With support and assistance from:
- Russian Ministry of Health Care and Social Development
- Russian Ministry of Industry and Trade
- Public Chamber of the Russian Federation
- Russian Academy of Medical Sciences

The Exhibition is held under the auspices of the Chamber of Commerce and Industry of the Russian Federation and the Government of Moscow.
IMPRINT

GERMAN MEDICAL JOURNAL
www.german-medical-journal.eu

PUBLISHER
BENNAD Ltd.
80637 München
Tel. +49 / (0)89 / 57 87 57 89
Fax. +49 / (0)89 / 13 16 30
info@bennad.com

SENIOR EDITOR
Nadine Baume
nb@bennad.com

EDITORIAL BOARD
Prof. Dr. rer. nat. Hans Fritz
Prof. Dr. med. Christian Sommerhoff

ADVISORY BOARD
Prof. Dr. med. Andreas B. Imhoff
Prof. Dr. med. Wiener Knopp
Prof. Dr. med. Alfred Königsrainer
Prof. Dr. med. Rüdiger Lange
Prof. Dr. med. Dr. (Lond.) Chris P. Lohmann
Prof. Dr. med. Felix Schier
Prof. Dr. med. Petra-Maria Schurr-Möhlmann
Prof. Dr. med. Jörg-Christian Tonn
Prof. Dr. med. Volker Tronnier
Univ.-Prof. Dr. med. Dr. h.c. D. Tschöpe

TRANSLATIONS
English:
Rene Kottke
Russian:
Fa. Medvoyage

ART DIRECTION / PRODUCTION
Linea Nova Ltd.
info@linea-nova.com
www.linea-nova.com

ADVERTISEMENTS
www.german-medical-journal.eu
adverts@gmjournal.com
Tel. +49 / (0)89 / 57 87 57 89
Fax. +49 / (0)89 / 13 16 30

SUBSCRIPTION
www.german-medical-journal.eu
subscription@gmjournal.com
Fax. +49 / (0)89 / 13 16 30

Neithr the editors nor the publisher can guarantee that all publications are correct. As soon as the author hands over his/her manuscript and illustrations, he/she authorizes their editing and publication. Unmarked photos and illustrations were given to the publisher by the respective authors. No guarantee for unsolicited manuscripts, photos and illustrations. Re-prints or reproduction of any kind – even in parts – may only be made with written permission of the publishing house and are subject to remuneration. In case of force majeure or disturbance of the industrial labour peace no claims for shipment or reimbursement arise.

Copyright 2010
Bennad Ltd.
All rights reserved
ISSN 1869-7836
peer-reviewed

To promote your company/hospital please contact:
Tel: +49 - (0)89 - 57 87 57 89
service@gmjournal.com
www.german-medical-journal.eu
Introduction and Epidemiology

Diverticular disease is very common in the developed world. The prevalence of asymptomatic diverticulosis is 5-10% before age 50, 30% after age 50, 50% after age 70 and 66% after age 85 [1, 2]. 20% of those patients will develop symptomatic diverticulitis. During the last 20 years, rates of admission and surgical interventions due to diverticulitis have increased, showing a rise of incidence [3]. In developed countries, the incidence of perforation of sigmoid diverticula is estimated with 2.4 in 100,000 [4]. There is no gender-related difference, but known risk factors for developing diverticula are age, low fiber diet, physical inactivity, constipation, obesity and smoking. Nonsteroidal anti-inflammatory drugs may increase the risk of perforation. In contrast to sigmoid diverticulosis as it is common in Western countries, right sided colonic diverticolosis in the absence of elevated intraluminal pressure is predominant in Asian countries. These form is assumed as a distinct entity of diverticulosis and shows rather hemorrhage than perforation as complications [3].

Pathogenesis

A diverticulum represents a saclike protrusion in the colonic wall that develops as a result of herniation of the mucosal and submucosal layer through weak points in the muscular wall of the colon. These diverticula are called pulsion or false diverticula (pseudo diverticula), because they do not contain all colonic wall layers. Diverticulosis describes the presence of multiple diverticula and generally correlates with an absence of symptoms [5](Fig. 1). Reasons for developing pseudo diverticula are high intraluminal pressure in combination with impairment of connective tissue, like it occurs commonly in elderly and constipated patients. The sigmoid as a high pressure zone of the intestine with its low compliance is predisposed to the formation of diverticula. Reduced volume stools are thought to contribute to elevated intracolonic pressure by enhanced peristaltic

Введение и эпидемиология

Дивертикулярная болезнь очень распространена в развитых странах мира. Распространенность бессимптомного дивертикулеза составляет 5-10% в возрасте до 50 лет, 30% после 50 лет, 50% после 70 лет и 66% после 85 лет [1, 2]. У 20% пациентов может развиться симптоматический дивертикулез. В течение последних 20 лет количество поступлений в стационар и хирургических вмешательств в связи с дивертикулезом увеличилось, подтверждая рост заболеваемости [3]. В развитых странах частота случаев перфорации дивертикула сигмовидной кишки оценивается как 2,4 на 100000 [4]. Не выявлено гендерных различий, широко известными факторами риска развития дивертикулов являются: возраст, диета с низким содержанием клетчатки, отсутствие физической активности, запоры, ожирение и курение. Нестероидные противовоспалительные препараты могут увеличивать риск перфорации. В отличие от дивертикулоза сигмовидной кишки, который часто встречается в западных странах, в странах Азии преобладает дивертикулез правых отделов толстой кишки без увеличения внутрипросветного давления в кишечнике. Эти формы выделена как отдельная нозологическая единица и чаще осложняется кровотечением, чем перфорацией [3].

Патогенез

Дивертикул определяется как мешочкоподобное выпячивание в стенке толстой кишки, которое развивается в результате грыжи слизистого и подслизистого слоев через слабые места в мышечной стенке толстой кишки. Подобные дивертикулы называются пульсионными или ложным дивертикулами (псевдодивертикулами), потому что они не содержат всех слоев толстой кишки. Дивертикулез подразумевает наличие множества дивертикулов, и, как правило, коррелирует с отсутствием симптомов [5] (рис. 1). Причиной для развития псевдо-дивертикулов является высокое внутрипросветное давление в сочетании с нарушением соединительной ткани, что характерно для лиц пожилого возраста и пациентов с запорами. Сигмовидная кишка как зона с высоким внутрипросветным давлением и низкой растяжимостью пред-
segmentation movements of the colon. Low-residue diet allows for exaggerated contractions of the colon, raising the intracolonic pressure and leading to an elevated motility index (product of amplitude and duration of activity) [1, 5]. Furthermore, altered neuromuscular activity may play a role. Once formed, diverticula will not disappear again, but the main concern is the interindividual difference in becoming symptomatic for diverticular disease. Diverticular disease occurs with the rise of symptoms. A subgroup is diverticulitis, which describes the presence of an inflammatory process associated with diverticula. The exact mechanism of inflammation of the diverticula is uncertain. Stasis and obstruction by a fecalith in the herniated part of the mucosa may lead to increased secretion of mucus and bacterial overgrowth. Thus, distension and erosion of the thin walled diverticulum can occur, leading to local tissue ischemia, suggesting pathogenetic features similar to appendicitis [2].

Increased levels of inflammatory mediators and proinflammatory cytokines result in mucosal inflammation [1]. Local inflammation may recede again by itself or under antibiotic treatment. Otherwise, it can lead to peridiverticulitis, which in turn can spread and lead to pericolitis. Then, formation of abscess or perforation with resulting peritonitis can occur.

Perforated diverticula are re-closing successively – otherwise leading to fecal peritonitis. Other theories of diverticulitis concern altered colonic flora, low grade chronic inflammation, periods of exacerbation and remission and indicate similarities to inflammatory bowel disease [1]. Bacterial flora in patients with low fiber diet is known to be decreased and altered as compared to patients eating high fiber [6]. Segmental colitis associated with diverticula (SCAD) is a term often mentioned in this context. Generally accepted as a distinct clinicopathologic entity, SCAD describes a focal chronic colitis characteristically involving the interdiverticular space, but sparing the diverticula themselves [7]. SCAD is known to be a risk factor for developing inflammatory bowel disease later on. There is also an overlap and association of diverticulitis and inflammatory bowel disease [6].

Clinical Presentation

Diverticulitis typically occurs in the elderly. With more than 95% of the cases, the sigmoid colon is the site by far most often affected of diverticulosis [2]. Concomitant involvement of the more proximal colon may be present; rectal diverticulitis is very uncommon. Asymptomatic diverticula are often diagnosed coincidentally during routine colonoscopy. Symptoms occur with the development of inflammation and include subfebrile temperature, tenderness, and sometimes a palpable resistance located in the left lower quadrant (clinically referred as “left sided appendicitis”). Cramps and irregular bowel movement (obstipation, diarrhea, bloating and flatulence) may also be present. Appearance and course of the diverticular disease is determined by the presence of an inflammatory process, which in turn can spread and lead to peritonitis. Then, formation of abscesses and perforation with peritonitis occurs. Perforated diverticula are re-closing successively – otherwise leading to fecal peritonitis. Other theories of diverticulitis concern altered colonic flora, low grade chronic inflammation, periods of exacerbation and remission and indicate similarities to inflammatory bowel disease [1]. Bacterial flora in patients with low fiber diet is known to be decreased and altered as compared to patients eating high fiber [6]. Segmental colitis associated with diverticula (SCAD) is a term often mentioned in this context. Generally accepted as a distinct clinicopathologic entity, SCAD describes a focal chronic colitis characteristically involving the interdiverticular space, but sparing the diverticula themselves [7]. SCAD is known to be a risk factor for developing inflammatory bowel disease later on. There is also an overlap and association of diverticulitis and inflammatory bowel disease [6].

Clinical Presentation

Diverticulitis typically occurs in the elderly. With more than 95% of the cases, the sigmoid colon is the site by far most often affected of diverticulosis [2]. Concomitant involvement of the more proximal colon may be present; rectal diverticulitis is very uncommon. Asymptomatic diverticula are often diagnosed coincidentally during routine colonoscopy. Symptoms occur with the development of inflammation and include subfebrile temperature, tenderness, and sometimes a palpable resistance located in the left lower quadrant (clinically referred as “left sided appendicitis”). Cramps and irregular bowel movement (obstipation, diarrhea, bloating and flatulence) may also be present. Appearance and course of the diverticular disease is determined by the presence of an inflammatory process, which in turn can spread and lead to peritonitis. Then, formation of abscesses and perforation with peritonitis occurs. Perforated diverticula are re-closing successively – otherwise leading to fecal peritonitis. Other theories of diverticulitis concern altered colonic flora, low grade chronic inflammation, periods of exacerbation and remission and indicate similarities to inflammatory bowel disease [1]. Bacterial flora in patients with low fiber diet is known to be decreased and altered as compared to patients eating high fiber [6]. Segmental colitis associated with diverticula (SCAD) is a term often mentioned in this context. Generally accepted as a distinct clinicopathologic entity, SCAD describes a focal chronic colitis characteristically involving the interdiverticular space, but sparing the diverticula themselves [7]. SCAD is known to be a risk factor for developing inflammatory bowel disease later on. There is also an overlap and association of diverticulitis and inflammatory bowel disease [6].

Clinical Presentation

Diverticulitis typically occurs in the elderly. With more than 95% of the cases, the sigmoid colon is the site by far most often affected of diverticulosis [2]. Concomitant involvement of the more proximal colon may be present; rectal diverticulitis is very uncommon. Asymptomatic diverticula are often diagnosed coincidentally during routine colonoscopy. Symptoms occur with the development of inflammation and include subfebrile temperature, tenderness, and sometimes a palpable resistance located in the left lower quadrant (clinically referred as “left sided appendicitis”). Cramps and irregular bowel movement (obstipation, diarrhea, bloating and flatulence) may also be present. Appearance and course of the diverticular disease is determined by the presence of an inflammatory process, which in turn can spread and lead to peritonitis. Then, formation of abscesses and perforation with peritonitis occurs. Perforated diverticula are re-closing successively – otherwise leading to fecal peritonitis. Other theories of diverticulitis concern altered colonic flora, low grade chronic inflammation, periods of exacerbation and remission and indicate similarities to inflammatory bowel disease [1]. Bacterial flora in patients with low fiber diet is known to be decreased and altered as compared to patients eating high fiber [6]. Segmental colitis associated with diverticula (SCAD) is a term often mentioned in this context. Generally accepted as a distinct clinicopathologic entity, SCAD describes a focal chronic colitis characteristically involving the interdiverticular space, but sparing the diverticula themselves [7]. SCAD is known to be a risk factor for developing inflammatory bowel disease later on. There is also an overlap and association of diverticulitis and inflammatory bowel disease [6].

Clinical Presentation

Diverticulitis typically occurs in the elderly. With more than 95% of the cases, the sigmoid colon is the site by far most often affected of diverticulosis [2]. Concomitant involvement of the more proximal colon may be present; rectal diverticulitis is very uncommon. Asymptomatic diverticula are often diagnosed coincidentally during routine colonoscopy. Symptoms occur with the development of inflammation and include subfebrile temperature, tenderness, and sometimes a palpable resistance located in the left lower quadrant (clinically referred as “left sided appendicitis”). Cramps and irregular bowel movement (obstipation, diarrhea, bloating and flatulence) may also be present. Appearance and course of the diverticular disease is determined by the presence of an inflammatory process, which in turn can spread and lead to peritonitis. Then, formation of abscesses and perforation with peritonitis occurs.
Fig. 1: Sigmoid diverticulosis
ease differ between patients. Presentation of diverticulitis can be acute or chronic. Acute cases of diverticulitis are classified as uncomplicated or complicated, depending on the severity of clinical presentation and radiologic findings. Complicated diverticulitis is defined as presence of abscess, phlegmon, fistula (mainly from the colon to the bladder), stricture, bowel obstruction, perforation and peritonitis [1, 2, 7]. Most perforations are small and sealed by pericolic fat, causing a circumscribed pericolic abscess (Hinchey stage II)[3]. Chronic diverticulitis can range between asymptomatic disease, mild intermittent manifestations or chronic distressing pain and permanent presence of symptoms [1].

Diverticular hemorrhage occurs in 3-5% of patients with otherwise asymptomatic diverticula and is the most common cause of colonic bleeding in western countries [6]. Up to 10% of patients require surgical intervention upon their first hospitalization. 1-2% show initial signs of free perforation with peritonitis, making emergency surgery necessary. In contrast, most patients can successfully be treated conservatively for their first attack of diverticulitis. About 25% of patients will have at least one episode of recurrence, most of them within one year after initial presentation. 5% develop more than one episode of recurrence.

For complicated diverticulitis, there is an estimated recurrence rate of 2% per patient year [3]. With an initial episode of uncomplicated diverticulitis, patients are unlikely to develop complicated diverticular disease in the further course [1,4].

Diagnosis
Computed tomography (CT) with intravenously applied contrast agent and rectal water-soluble contrast enema is recommended as the initial radiological examination. Colonoscopy is not advised during acute diverticulitis due to the risk of perforation [2]. On blood level, leukocytosis and elevated C-reactive protein (CRP) are common. Colorectal carcinoma, irritable bowel syndrome, inflammatory bowel disease (especially in the presence of fistula) and gynecological diseases like adenitis or ectopic pregnancy have to be considered as possible alternative diagnoses. Especially in young women, who have a wide range of differential diagnoses, diverticulitis is possibly not considered initially, delaying treatment and worsening outcome [3].

Staging of Diverticulitis
While the diagnosis of acute diverticulitis is usually easy to confirm, detemining the severity of the current attack is significantly more difficult but

<table>
<thead>
<tr>
<th>Classification of Hinchey</th>
<th>Table 1: Classification of Hinchey</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hinchey I  Localized abscess (pericolic or in mesocolic)</td>
<td></td>
</tr>
<tr>
<td>Hinchey II  Pelvic or retroperitoneal abscess</td>
<td></td>
</tr>
<tr>
<td>Hinchey III  Generalized purulent peritonitis (non-communicating peritonitis)</td>
<td></td>
</tr>
<tr>
<td>Hinchey IV  Generalized feculent peritonitis (communicating peritonitis)</td>
<td></td>
</tr>
</tbody>
</table>

Table 1: Classification of Hinchey

<table>
<thead>
<tr>
<th>Таблица 1: Классификация Hinchey</th>
</tr>
</thead>
</table>

Симптомы появляются при развитии воспаления и включают субфебрильную температуру, болезненность при пальпации, а иногда и выраженную резистентность брюшной стенки в левом нижнем квадранте, клинически симулирующую «левосторонний аппендицид». Могут отмечаться судороги и нерегулярный стул (запоры, диарея, вздутие живота и метеоризм). Возникновение и течение дивертикулярной болезни отличается у каждого отдельного пациента. Течение дивертикулеза может быть острым и хроническим. Острый дивертикулез разделяют на неосложненную или осложненную форму в зависимости от тяжести клинической картины и результатов radiологического исследования. Осложненный дивертикулез характеризуется наличием абсцесса, флегмоны, свища (в основном, из толстой кишки в мочевой пузырь), структуры, непроходимости кишечника, перфорации и перитонита [1, 2, 7]. Большинство перфораций небольшие и закрываются околосшечечными жировыми, вызывая ожоговые абсцессы (I стадия по Hinchey) [3]. Хронический дивертикулез может варьировать от бессимптомной формы, с незначительными проявлениями, до формы с мучительными болями и постоянными симптомами [1].

Дивертикулярное кровотечение происходит у 3-5% пациентов с бессимптомным течением заболевания и является наиболее распространенной причиной кровотечения из толстой кишки в западных странах [6]. До 10% пациентов требуется хирургическое вмешательства уже при первой госпитализации. У 1-2% пациентов отмечаются первые признаки перфорации с перитонитом, что делает необходимым срочную операцию. Однако, большинство пациентов при первом проявлении дивертикулеза можно успешно лечить консервативными методами. У 25% пациентов отмечается один эпизод рецидива, в большинстве случаев он наступает течение одного года после первого проявления заболевания. У 5% пациентов отмечается более одного эпизода рецидива. Для осложненного дивертикулеза, показатель возникновения рецидива составляет 2% в год [3]. В случае первого эпизода в виде неосложненного дивертикулеза, у пациента в ряду ли в дальнейшем развивается осложненный дивертикулез [1, 4].

Диагностика
Компьютерная томография (КТ) с внутривенным введением контрастного средства и ректальной кишкой с водорастворимым контрастом рекомендуется в качестве начального радиологического обследования. Колоноскопия при остром дивертикуле не рекомендуется из-за риска перфорации [2]. В крови отмечается лейкоцитоз и повышение уровня С-реактивного белка. Колоректальный рак, синдром раздраженного кишечника, воспалительные заболевания кишечника (особенно при наличии свища) и гинекологические
remains essential for stratification of further therapy [1]. A large number of more or less identical classification systems have emerged in the last decades with the aim of staging diverticular disease and providing sufficient therapeutic algorithms. An early and widely accepted classification system for perforated diverticulitis was proposed by Hinchev et al. in 1978 (table 1)[8]. Developed before routine diagnostic CT scans found the way into clinical practice, it is based on intraoperative findings.

A scoring systems with high grade of clinical relevance was suggested by Hansen and Stock (table 2) [9]. Based on pre-therapeutical clinical findings, it allows stratification into different risk and treatment groups.

**Therapy**

Acute diverticulitis without perforation is generally treated non-operatively, which means dietary restriction and antibiotics. For a long time, the rule was to remove the affected bowel segment when the second attack of diverticulitis occurs [3]. In the last years, the general opinion in the treatment of recurrent sigmoid diverticulitis started to change and the role of surgery is declining in favor to conservative treatment. Recent data show that surgical intervention for complications becomes necessary at initial manifestation of diverticular disease about two or three times more frequent than in recurrent episodes [10]. Furthermore, mortality is higher in patients on their first onset or three times more frequent diverticular disease about two necessary at initial manifestation of complications becomes necessary for perforation. Recent data show the necessity of surgery. Rather, clinical graduation of seriousness and individual aspects should to be considered.

**Acute Uncomplicated Diverticulitis**

When the inflammatory process is limited to the bowel wall, wide spectrum antibiotics in combination with light, low fiber diet are sufficient as initial approach. In otherwise healthy patients with only mild symptoms, oral drug administration in an outpatient setting can be performed. Typical antibiotics are metronidazole in combination with ciprofloxacin or amoxicillin-clavulanate for 1-2 weeks [2, 7]. Hospital admission with close surveillance and intravenously administration of antibiotics becomes necessary in systemically ill, immunocompromised or elderly patients or if patients have significant symptoms compared to relapse cases. Failure of initial started conservative treatment is about 10-20% and does not change with the number of episodes [2]. Therefore, the number of experienced episodes is not appropriate for indication of surgery. Rather, clinical graduation of seriousness and individual aspects should to be considered.

<table>
<thead>
<tr>
<th>Classification of Hansen and Stock</th>
<th>Asymptomatic diverticulosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>Hansen-Stock 0</td>
<td>Acute uncomplicated diverticulitis</td>
</tr>
<tr>
<td>Hansen-Stock 1</td>
<td>Acute complicated diverticulitis</td>
</tr>
<tr>
<td>Hansen-Stock 2</td>
<td>Peridiverticulitis / phlegmonous diverticulitis</td>
</tr>
<tr>
<td>2a</td>
<td>Covered perforation, mesenteric abscess</td>
</tr>
<tr>
<td>2b</td>
<td>Free perforation, generalized purulent peritonitis</td>
</tr>
<tr>
<td>Hansen-Stock 3</td>
<td>Recurrent diverticulitis</td>
</tr>
</tbody>
</table>

Table 2: Classification of Hansen and Stock

Таблица 2: Классификация Hansen и Stock

Балльная система, которая имеет большое значение в клинической практике, была предложена Hansen и Stock (таблица 2) [9]. Базирующаяся на предварительных клинических данных, она позволяет распределить пациентов по разным группам риска и лечения.

**Терапия**

Острый дивертикулез без перфорации, как правило, лечится консервативно, с помощью диет и антибиотиков. Долгое время было правилом удаление по-рожденного сегмента кишечника при втором обострении дивертикулеза [3]. В последние годы, мнение специалистов о лечении рецидивирующего дивертикулеза симптоматичной кишки изменилось — возрастает роль консервативного лечения. Последние данные показывают, что необходимость хирургического вмешательства при осложнениях возникает при начальных проявлениях дивертикулеза в 2-3 раза чаще, чем при рецидивах [10]. Кроме того, показатель смертности выше у пациентов при первом проявлении заболевания по сравнению с рецидивами. Неэффективность начального консервативного лечения составляет около 10-20% и не растет с увеличением количества рецидивов [2]. Таким образом, увеличение числа рецидивов не является показанием к операции. Скорее, должны учитываться степень клинические проявлений и индивидуальные особенности каждого конкретного случая.

**Острый несложенный дивертикулез**

Когда воспалительный процесс ограничивается стенкой кишеч-
7]. The apparently higher mor-

evidence for this strategy [1, 3,

to these patients. But there is no

litis has been proposed for

the first episode of diverticu-

Thus, surgical resection after

risk of a complicated course.

larger abscesses usually re-

percutaneous CT guided

in that case, elective

surgery should be performed

3-4 weeks after drainage due
to the high risk of recurrent

diverticulitis [7]. If the abscess

is not accessible for interven-
tional drainage because of its

anatomical localization, prompt

surgery becomes necessary.

Diverticular disease in young

patients under 40-50 years of

age is sometimes described

as specific entity with a higher

risk of a complicated course.

Thus, surgical resection after

the first episode of diverticu-
litis has been proposed for

these patients. But there is no

evidence for this strategy [1, 3,

7]. The apparently higher mor-
bidity may be due to the long

follow-up in these patients and

because of delayed diagnosis
due to uncommon clinical pres-

tentation [7]. However, special

remark applies for the immu-
nocompromised. It is not clear

whether these patients have

an elevated risk to develop

diverticulitis, but their episodes

are more likely to be compli-
cated [1]. Therefore, in patients

with risk factors like taking
corticosteroids, immunosup-

pressive therapy after organ

transplantation, HIV or dia-

teses, colectomy is warranted

after the first attack of diver-
ticulitis in order to anticipate

further complications [1,2,7].

Acute Complicated
Diverticulitis

Complicated forms of diver-
ticulitis require intravenously

antibiotics, bowel rest and pain

control [1]. In addition, percuta-

aneous drainage of abscess or

surgery is necessary in most

cases. Emergency surgery is

indicated for generalized peritonitis, uncontrolled sepsis, bowel perforation, the pres-

cence of large not drainable

abscess or if symptoms cannot

get under control by antibiotic


treatment [10]. If complicated

diverticulitis can be success-

fully treated conservatively,

patients should undergo opera-

tion after the first attack.

The surgical procedure in-
cludes the removal of the

inflammation bearing colon

segment (usually the sigmoid

colon, Fig. 2). Resection of

additional, asymptomatic
diverticula in other bowel parts

is not necessary. The most im-

portant segment is the sigmoid

colon as the primary region

of high pressure in the colon.

Though, leaving a diverticula

bearing segment in situ in this

bowel region or inclusion of

any diverticula into a stapled

anastomosis must be avoided

[7]. Depending on the extent of

local inflammation, a passager

diverting stoma may be indi-
cated, which will be reversed

after 2-3 months. However,

usually no diverting stoma is

indicated.
Fig. 2: Resection of the diverticula bearing sigmoid
Formerly, a traditional three stage procedure was performed depending on the grade of local inflammation or peritonitis (1st, diverting stoma, 2nd, resection of the diseased colon followed by anastomosis, 3rd, reversal of the ostomy)[2]. Overall mortality for this three stage approach was up to 25%[3] and in about 50%, these stomas were never restored again. For distinct patients with severe peritonitis or sepsis (Hinchey IV), still sigmoid resection with Hartmann’s procedure and colonostomy is indicated. The stoma is reversed after 2-3 months. Today, in most of the patients with severe and complicated diverticulitis, a two stage procedure with resection and colonostomy (1st) that is closed after 8-12 weeks[2nd][6] or even a single-stage approach without any colonostomy is possible and safe [1, 3].

Chronic Diverticulitis

A challenging subgroup of patients are those with chronic low-level symptoms. These patients have low rates of morbidity or complicated courses, but may suffer remarkable impairment of quality of life. Therefore, postoperative quality of life and release of discomfort and not anticipation of complications play the main role when considering adequate therapy for those patients [1, 3]. Disarrangement of microbacterial milieu and chronic inflammation may be causal for symptoms. New approaches consider probiotic therapy (e.g., with Escherichia coli Nissle 1917) and anti-inflammatory drugs known from inflammatory bowel disease (e.g., mesalazine) as possible treatment option [3, 6]. Being aware of potential deterioration of the diverticular disease, in patients with mild but chronic symptoms, these therapeutic strategies can be a promising alternative as first instance of treatment.

The best moment for elective resection after recovery of diverticular disease remains controversial. Data show that complicated diverticulitis mainly arises already with the first attack and recurrent episodes usually do not become worse than the initial one [3]. Therefore, indication for elective resection is mainly based on individual aspects like general condition, concomitant diseases, distress and possible enhancement of quality of life after resection. The former rule to operate after the second attack does not apply any more [3]. Rather, decision should be made on a case-by-case basis with a careful risk-benefit assessment for every individual patient. There are suggestions for not operating before the fourth attack of uncomplicated diverticulitis, which results in abscesses or if symptoms do not improve after treatment with antibiотics [10].

Даже если осложненный дивертикулез можно успешно лечить консервативно, пациенты следуют провести оперативное лечение уже после первой атаки заболевания. Хирургическая процедура включает в себя удаление по- раженного воспалением сегмента толстой кишki (как правило, сигмовидной кишки, рисунок 2).

Резекция других, бессимптомных дивертикулов в других частях кишечника не является необходимым. Однако, известно, что наиболее ранимым участком является сигмовидная кишка в качестве основной области высокого давления в толстой кишке. Следовательно, оставление сегмента с дивертикулами in situ в этом регионе кишечника или включение любых дивертикулов в анестомоз следует избегать [7].

In the absence of local inflammation, the patient may be shown to have a colostomy, which can be closed after 2-3 months. It is then the opinion that the second attack does not require one more [3]. Rather, decision should be made on a case-by-case basis with a careful risk-benefit assessment for every individual patient. There are suggestions for not operating before the fourth attack of uncomplicated diverticulitis, which results in abscesses or if symptoms do not improve after treatment with antibiotics [10].

В зависимости от степени местного воспаления, может быть показано наложение колостомы, которая может быть закрыта через 2-3 месяца. Следует отметить, что, как правило, этого не требуется.

Ранее выполнялась традиционная трехэтапная операция в зависимости от степени местного воспаления или перитонита (1 - формирование стомы, 2 - резекция пораженной кишки с формированием анастомоза, 3 - закрытие стомы) [2]. Общая смертность для указанного трехэтапного подхода ставила до 25% [3], и, примерно, в 50% случаев проход в кишку не был восстановлен. Для ряда пациентов с тяжелым перитонитом или сепсисом (Hinchey IV), по-прежнему показана резекция сигмовидной кишки по методу Хартманна и колостома. Стoma закрывается через 2-3 месяца. Ныне, большинству пациентов с тяжелым течением дивертикулеза и осложнениями проводится двухэтапная операция с резекцией и формированием колостомы (1 этап), которая закрывается через 8-12 недель (2 этап) [6]. Возможен и безопасен одноэтапный подход без какой-либо колостомы [1, 3].

Хронический дивертикулез

К данной группе относятся пациенты, у которых отмечаются постоянные, но не резко выраженные симптомы. Для этих пациентов характерно легкое или среднетяжелое течение заболевания без осложнений, которое, однако, может значительно ухудшить качество жизни. Поэтому, обеспечение качества жизни после операции и снижение дискомфорта, а не профилактика осложнений являются целью адекватной терапии для таких пациентов [1, 3].

Причиной развития постоянных симптомов может быть нарушение бактериальной среды и хроническое воспаление. Новые подходы в лечении рассматривают пробиотическую терапию (например, с помощью Escherichia coli Nissle 1917) и противовоспалительные препараты, применяющиеся при воспалительных заболеваниях кишечника (например, месалазин) как возможный вариант лечения [3, 6].

Особая возможность исчезновения пациентов при хроническом дивертикулезе, эти терапевтические стратегии могут быть многообещающей альтернативой первоначального лечения.
Laparoscopic surgery is the standard procedure in the elective setting. It reduces pain, recovery time and causes a lower rate of morbidity [7]. A laparoscopic approach is also feasible for some forms of complicated diverticular disease. In general, it is advocated by many surgeons for Hinchey stage I and II disease, but less well accepted for Hinchey stage III and IV disease [2]. However, when conversion becomes necessary, early conversion can minimize morbidity. Possible minimal invasive techniques in general are straight laparoscopy, hand assisted and even single port access sigmoidectomy [7].

The best approach is still a matter of debate. We discuss surgery individually with every patient after a successful treatment of a diverticulitis attack, but are more restricted than in the past. Surgery should be performed after conservative treatment of a complicated diverticulitis attack, inability to exclude cancer, dependent of the patient’s symptoms, the frequency, persistence and severity of episodes, patient’s risk in regard to co-morbidities and age. A fibrotic stenosis after chronic recurrent diverticulitis is irreversible and should be resected surgically. Surgery is performed laparoscopically whenever possible.

References
Lung cancer is among the most frequent malignant diseases for men and women. Its frequency increases with age of the individuals. According to WHO more than one million people die worldwide from lung cancer every year. Causative for this high death toll in the majority of patients is cigarette smoking. Unfortunately, more than half of the patients are first diagnosed when the disease is already in a metastatic stage.

Diagnostics

The University Hospital of Münster (UKM) is one of Germany’s leading centers for multidisciplinary diagnostics and treatment of lung cancer (1). Our radiologists perform large population studies on the value of screening computer tomography in risk populations to possibly allow better prognosis by early diagnosis (2,3). All modern techniques for fast and patient-friendly diagnosis including FDG-PET-CT, CT-guided needle biopsy, flexible bronchoscopy with Endoscopic Bronchoscopic Ultrasound (EBUS; Fig. 1) and thoracoscopy are easily available. Patients can be diagnosed on an outpatient basis. The Gerhard-Domagk-Institute for Pathology provides a team of experienced lung pathologists for histological diagnosis and typing of the lung cancer. Today not only histology (small cell lung cancer vs. non-small lung cancer; adenocarcinoma vs. squamous cell carcinoma in the group of non-small cell lung cancer) is crucial for correct treatment, but also molecular pathology becomes more and more essential. Some tumors especially in the group of non-small lung cancers (NSCLC) are biologically greatly influenced by the gene copy number of, or specific mutations in the Epidermal Growth Factor-Receptor (EGF-R). This, and signalling pathways, such as the RAS-pathway with mutations in the RAS signalling molecule help select modern treatment components (Fig. 2).

Multimodal treatment approaches especially in non-small cell lung cancer (NSCLC) are highly dependent from the stage of the tumor, and the most mature version of the WHO TNM-staging system (FBC–UZI (Fig 1) and thoracoscopy. Patients can be diagnosed in ambulatory conditions. The Gerhard-Domagk-institute for Pathology provides a team of experienced lung pathologists for histological diagnosis and typing of the lung cancer. Today not only histology (small cell lung cancer vs. non-small lung cancer; adenocarcinoma vs. squamous cell carcinoma in the group of non-small cell lung cancer) is crucial for correct treatment, but also molecular pathology becomes more and more essential. Some tumors especially in the group of non-small lung cancers (NSCLC) are biologically greatly influenced by the gene copy number of, or specific mutations in the Epidermal Growth Factor-Receptor (EGF-R). This, and signalling pathways, such as the RAS-pathway with mutations in the RAS signalling molecule help select modern treatment components (Fig. 2).

Multimodal treatment approaches especially in non-small cell lung cancer (NSCLC) are highly dependent from the stage of the tumor, and the most mature version of the WHO TNM-staging system (FBC–UZI (Fig 1) and thoracoscopy. Patients can be diagnosed in ambulatory conditions. The Gerhard-Domagk-institute for Pathology provides a team of experienced lung pathologists for histological diagnosis and typing of the lung cancer. Today not only histology (small cell lung cancer vs. non-small lung cancer; adenocarcinoma vs. squamous cell carcinoma in the group of non-small cell lung cancer) is crucial for correct treatment, but also molecular pathology becomes more and more essential. Some tumors especially in the group of non-small lung cancers (NSCLC) are biologically greatly influenced by the gene copy number of, or specific mutations in the Epidermal Growth Factor-Receptor (EGF-R). This, and signalling pathways, such as the RAS-pathway with mutations in the RAS signalling molecule help select modern treatment components (Fig. 2).

Multimodal treatment approaches especially in non-small cell lung cancer (NSCLC) are highly dependent from the stage of the tumor, and the most mature version of the WHO TNM-staging system (FBC–UZI (Fig 1) and thoracoscopy. Patients can be diagnosed in ambulatory conditions. The Gerhard-Domagk-institute for Pathology provides a team of experienced lung pathologists for histological diagnosis and typing of the lung cancer. Today not only histology (small cell lung cancer vs. non-small lung cancer; adenocarcinoma vs. squamous cell carcinoma in the group of non-small cell lung cancer) is crucial for correct treatment, but also molecular pathology becomes more and more essential. Some tumors especially in the group of non-small lung cancers (NSCLC) are biologically greatly influenced by the gene copy number of, or specific mutations in the Epidermal Growth Factor-Receptor (EGF-R). This, and signalling pathways, such as the RAS-pathway with mutations in the RAS signalling molecule help select modern treatment components (Fig. 2).

Multimodal treatment approaches especially in non-small cell lung cancer (NSCLC) are highly dependent from the stage of the tumor, and the most mature version of the WHO TNM-staging system (FBC–UZI (Fig 1) and thoracoscopy. Patients can be diagnosed in ambulatory conditions. The Gerhard-Domagk-institute for Pathology provides a team of experienced lung pathologists for histological diagnosis and typing of the lung cancer. Today not only histology (small cell lung cancer vs. non-small lung cancer; adenocarcinoma vs. squamous cell carcinoma in the group of non-small cell lung cancer) is crucial for correct treatment, but also molecular pathology becomes more and more essential. Some tumors especially in the group of non-small lung cancers (NSCLC) are biologically greatly influenced by the gene copy number of, or specific mutations in the Epidermal Growth Factor-Receptor (EGF-R). This, and signalling pathways, such as the RAS-pathway with mutations in the RAS signalling molecule help select modern treatment components (Fig. 2).

Multimodal treatment approaches especially in non-small cell lung cancer (NSCLC) are highly dependent from the stage of the tumor, and the most mature version of the WHO TNM-staging system (FBC–UZI (Fig 1) and thoracoscopy. Patients can be diagnosed in ambulatory conditions. The Gerhard-Domagk-institute for Pathology provides a team of experienced lung pathologists for histological diagnosis and typing of the lung cancer. Today not only histology (small cell lung cancer vs. non-small lung cancer; adenocarcinoma vs. squamous cell carcinoma in the group of non-small cell lung cancer) is crucial for correct treatment, but also molecular pathology becomes more and more essential. Some tumors especially in the group of non-small lung cancers (NSCLC) are biologically greatly influenced by the gene copy number of, or specific mutations in the Epidermal Growth Factor-Receptor (EGF-R). This, and signalling pathways, such as the RAS-pathway with mutations in the RAS signalling molecule help select modern treatment components (Fig. 2).

Multimodal treatment approaches especially in non-small cell lung cancer (NSCLC) are highly dependent from the stage of the tumor, and the most mature version of the WHO TNM-staging system (FBC–UZI (Fig 1) and thoracoscopy. Patients can be diagnosed in ambulatory conditions. The Gerhard-Domagk-institute for Pathology provides a team of experienced lung pathologists for histological diagnosis and typing of the lung cancer. Today not only histology (small cell lung cancer vs. non-small lung cancer; adenocarcinoma vs. squamous cell carcinoma in the group of non-small cell lung cancer) is crucial for correct treatment, but also molecular pathology becomes more and more essential. Some tumors especially in the group of non-small lung cancers (NSCLC) are biologically greatly influenced by the gene copy number of, or specific mutations in the Epidermal Growth Factor-Receptor (EGF-R). This, and signalling pathways, such as the RAS-pathway with mutations in the RAS signalling molecule help select modern treatment components (Fig. 2).

Multimodal treatment approaches especially in non-small cell lung cancer (NSCLC) are highly dependent from the stage of the tumor, and the most mature version of the WHO TNM-staging system (FBC–UZI (Fig 1) and thoracoscopy. Patients can be diagnosed in ambulatory conditions. The Gerhard-Domagk-institute for Pathology provides a team of experienced lung pathologists for histological diagnosis and typing of the lung cancer. Today not only histology (small cell lung cancer vs. non-small lung cancer; adenocarcinoma vs. squamous cell carcinoma in the group of non-small cell lung cancer) is crucial for correct treatment, but also molecular pathology becomes more and more essential. Some tumors especially in the group of non-small lung cancers (NSCLC) are biologically greatly influenced by the gene copy number of, or specific mutations in the Epidermal Growth Factor-Receptor (EGF-R). This, and signalling pathways, such as the RAS-pathway with mutations in the RAS signalling molecule help select modern treatment components (Fig. 2).
been shown to improve survival time in randomized trial. Different TNM-stages can be grouped into a clinical staging system of four stages (I-IV; for further details see ref. 4). Whereas invasive mediastinoscopy is still considered as being standard in the staging diagnostics of mediastinal lymph node involvement, modern procedures combining methods of nuclear medicine and radiology such as Positron Emission Tomography (PET) - Computed Tomography (CT) more and more replace this invasive procedure by exact non-invasive diagnostics (Fig. 1b; 5,6).

Treatment
Whereas in the 25% of patients with small cell lung cancer (SCLC) surgery as a first treatment modality plays only a role in few patients with very early stages, systemic treatment with modern platinum-containing chemotherapy doublets and early radiotherapy together with best supportive care can increase survival time of most patients. Today prophylactic cranial irradiation (PCI) is even performed in patients with “extensive disease” with tumor deposits beyond one hemithorax, since this has been shown to improve survival time in randomized trial.

Contrary, for patients with NSCLC multimodal treatment, making excellent cooperation between surgeons, radiotherapists, pneumologists and medical oncologists necessary, is a pre-requisite for optimal prognosis in patients with all stages of disease. The multimodal treatment procedure is discussed upfront in an interdisciplinary tumor panel session.

In stage I (without lymph node involvement) and in stage II (including ipsilateral lymph node involvement) tumor surgery has curative potential. A radical surgical lymphadenectomy is an important factor and has prognostic relevance. Minimal-

Fig. 1: EBUS-TBNA. (a) Flexible bronchoscopy can be used to perform an endoscopy bronchoscopic (EB) ultrasound (US). This techniques allows to perform a transbronchial needle aspiration (TBNA) of a lymph node suspicious for malignant cells. (b) Using a PET-CT scan, a high glucose uptake (yellow color) indicating metabolically active cells could be visualised in a right paratracheal dorsal lymph node. (c) The diameter of the target structure was 26 mm (blue line) as visualized with EBUS. (d) The transbronchial needle aspiration (arrows) was monitored in real-time with EBUS.

Рис 1: ФБС–УЗИ (a) Фиброскопы могут быть использованы для выполнения эндоскопического бронхоскопического (ФБС) ультразвука (УЗИ). Этот метод позволяет выполнить трансбронхиальную аспирационную биопсию (ТБАБ) из подозрительных на злокачественные клетки лимфоузлов. (b) С помощью PET-КТ сканирования и использования феномена усиленного поглощения глюкозы (желтый цвет) метаболически активные клетки были визуализированы в правом паратрахеальном дорсальном лимфоузле. (c) Диаметр изучаемой структуры составил 26 мм (синяя линия) визуализированный ФБС–УЗИ. (d) Трансбронхиальная аспирационная биопсия (показана стрелками) была проведена под контролем ФБС–УЗИ в режиме реального времени.

Последняя версия классификации опухолового процесса по системе TNM, разработанная Всемирной организацией здравоохранения (ВОЗ). Различные TNM-стадии рака могут быть сгруппированы в 4 клинические стадии рака (I-IV)(4).

В последнее время инвазивные методы обследования, например, медиастиноскопия, (по-прежнему рассматривается как стандартный метод для исследования медиастинальных лимфатических узлов), замещаются на более точные и неинвазивные методы, такие как ПЭТ / КТ (позитронно-эмиссионная томография / компьютерная томография) (Рис 1b)(5, 6).

Лечение
Только 25% пациентов с мелкоклеточным раком легких (МРЛ) показано комбинированное лечение (хирургия, химиотерапия, лучевая терапия), что может быть обеспечено только четким взаимодействием онколога, пульмонолога, радиолога и онколога и составлением общего плана лечения на всех стадиях заболевания. Такой план лечения обсуждается на междисциплинарном консультум с участием всех специалистов.

На стадии I (без поражения лимфатических узлов), а в стадии II (в том числе с поражением ipsilateralных лимфатических узлов) хирургическое лечение опухоли имеет значительный лечебный потенциал. Радикальное хирургическое иссечение лимфатических узлов (лимфаденэктомия) является
invasive approaches and sleeve resection techniques improve recovery following surgery and allow for surgical resections even in patients with severely reduced lung function. Also, definitive radiotherapy using stereotactic irradiation techniques may be taken into account, when surgery is inappropriate for several reasons.

According to international trials no adjuvant radiotherapy is been given, but for patients with stage II platinum containing adjuvant (postoperative) chemotherapy can improve the prognosis. Randomized trials have shown that preoperative chemotherapy is a standard for operable stage III patients and almost every patient earlier or later needs radiotherapy.

In stage III with ipsilateral (IIIA) or contralateral (IIIB) mediastinal lymph node involvement surgery find its limits in accordance with the experience of the thoracic tumor surgery team in place. Radiochemotheraphy is the treatment of choice in inoperable stage III patients. The optimal choice and sequence of the three classical treatment modalities in stage III is still a matter of trials. The UKM coordinates studies for optimization of treatment within the German Lung Cancer Cooperative Group (7).

Modern techniques for radiotherapy have greatly improved the efficacy and tolerability of this treatment modality. Up-to-date technology with tomotherapy provides a technique, in which the radiotherapy source is circling around a patient (Fig. 3). Tomotherapy provides the opportunity of continuous image-guided control of radiotherapy by cone beam CT during radiation, it is not only a great step forward for patients with lung cancer but also with mesothelioma of the pleura and mediastinal tumors of other histology. Radiation of single brain metastasis with this technique is even possible without hair loss, which often in a palliative situation is of great value, especially for female patients. Tomotherapy also allows a better radiation intensity for small-volume tumors with a stereotactic hypofractionated therapy modification. This can be used for radiation of lung metastases. By the continuous

Fig. 2: Molecular Pathology of EGFR and k-RAS showing therapy-relevant mutations by sequencing. Рис 2: Молекулярная диагностика. Определение EGFR и k-RAS для составления плана лечения.

На стадии III с поражением ipsilateralных (IIIA) или contralateralной (IIIB) лимфоузлов средостения возможности хирургического лечения ограничены. Оперативное лечение может быть проведено при наличие у хирурга достаточного опыта. Комбинированная радиохимиотерапия является методом выбора для неоперабельных пациентов на III стадии.

Оптимальный выбор и последовательность всех трех классических методов лечения пациентов со стадией III по-прежнему определяется в ходе клинических испытаний.

Университетская клиника Мюнхена в составе германской Группы по изучению рака легких координирует клинические испытания по оптимизации лечения (7).

Современные технологии лучевой терапии значительно улучшили эффективность и переносимость этого метода лечения. При использовании новейшей системы лучевого лечения «ТомоТерапия», источник облучения кружится вокруг пациента (Рис 3). «ТомоТерапия» обеспечивает возможность непрерывного контроля пучка облучения посредством передачи изображения облучаемых структур на источник излучения, что дает огромные преимущества при лечении больных не только с
movement of the modulated fan beam around the patient the toxicity for the surrounding tissue can be minimized.

As mentioned above the majority of patients is first diagnosed with metastatic disease. In particular the prognosis of patients with late stage III or stage IV of NSCLC with distant metastasis is still dismal. However, multimodal therapy including biological treatment, chemotherapy and radiotherapy can improve survival time and quality of life. Today it is of utmost importance to perform molecular diagnosis in the tumor material of every patients before treatment onset. Some patients, especially without any smoking history and in the group of adenocarcinoma do not necessarily have to undergo chemotherapy as the first treatment in case they show specific EGF-R mutations (Fig. 2). This small group of patients (approximately 10 to 20%) undergo modern treatment with orally applied receptor tyrosine kinase inhibitors (8). In particular, patients with undisturbed signaling pathways, e.g. without activating mutations in the RAS-molecule, seem to benefit from this treatment with some of the tumors showing a good response (9).

In the other patients standard histology discerning between
adenocarcinoma and other histologies of NSCLC can help selecting chemotherapeutic compounds for first line treatment. Platinum based doublets are standard for patients with good performance status and according to a randomized trial pemetrexed in combination with platinum shows some advantage for patients with adenocarcinoma. Addition of the anti-VEGF-antibody bevacizumab to chemotherapy can further prolong survival in patients with adenocarcinoma. Palliative radiotherapy often is important in patients with metastatic disease for improvement of quality of life and one example is the radiation of metastatic deposits causing pain for the patient. In addition, each patient needs “best supportive care” and the offer of psychoncology support (10) to improve quality of life and particularly adequate pain medication is necessary. Often tumor related symptoms are caused by partial or complete obstruction of airways through tumor deposits. In these cases local treatment with modern techniques of pneumology, such as afterloading irradiation (brachytherapy, intraluminal radiation), argon plasma coagulation, laser therapy, cryotherapy, stenting and combinations thereof can reduce symptoms and inhibit the development of post-stenosis related complications, such as pneumonia (Fig. 4). Also for this reason it is of advantage that patients are taken care of by a team of pneumologists and medical oncologists with double specialization.

Fig 4: Endobronchial stents to circumvent airway stenosis. A 21-year old patient presented with severe shortness of breath. Bronchoscopy revealed malignant stenosis in the (a) proximal trachea, (b) right main bronchus, and (c) left lower bronchus (LLB). (d) Chest X-ray demonstrated the successful application of two airway stents. First, a nitinol stent was placed in the LLB (light blue arrows). Using a carina Y-stent, both stenosis in the right main bronchus and the trachea could be circumvented (white arrows). (e) Intraluminal endoscopic view of Y-stent in situ on top of the carina (C), branching into left (l.) main bronchus and right (r.) main bronchus. To facilitate repetitive systemic therapies, a port system was implanted.

Рис 4: Эндобронхиальные стенты для расширения участка стеноза дыхательных путей у 21-летнего пациента с тяжелой одышкой. Бронхоскопия выявила стеноз за счет опухолевого процесса (a) проксимальной трахеи, (b) правого главного бронха, и (c) левого нижнего бронха (d) Рентген грудной клетки показывает успешное стентирование двух дыхательных путей: нитиноловый стент был помещен в левый нижний бронх (отмечено светло-голубыми стрелками), использован килеобразный Y-стент для расширения участка стеноза правого главного бронха и трахеи (отмечено белыми стрелками). (e) Вид изнутри Y-стента в области верхушки киля при эндоскопии (c), Разветвление его на левый главный бронх (l) и на правый главный бронх (r). Для проведения повторной терапии имплантирована портальная система.

Рак легкого при первом обращение в случае, если они у них отмечается специфическая мутация EGF-R фактора (Рис. 2). Эта небольшая группа больных (приблизительно от 10 до 20%) получает лечение посредством перорального приема ингибиторов рецепторов тирозинкиназа и дают хороший ответ на лечение. Дифференциальная гистологическая диагностика между adenокарциномой и другими гистологическими вариантами НМРЛ может помочь в выборе химиотерапевтических препаратов для лечения первой линии.

Двухкомпонентная химиотерапия (Пеметрексед + Платиносодержащий препарат) является стандартом лечения для пациентов с их хорошей переносимостью и, согласно рандомизирован-
Prognosis

As the majority of patients is diagnosed in a metastatic state, prognosis of lung cancer today is still dismal. Five-year survival is less than 20% in patients with metastatic disease stages. Since more than 80% of lung cancers are caused by smoking, anti-smoking teaching and anti-smoking campaigns may greatly help to reduce the burden of this malignant disease for our population. Programs to start this kind of prophylactic teaching already begin in the school age working with children.

In summary although deep cuts into the incidence, mortality and lethality of lung cancer are still an unfulfilled objective of joint forces in health care, prognosis and quality of life of individual patients suffering from lung cancer can greatly improve by modern interdisciplinary oncology patient care.

References:

или полным блокированием дыхательных путей. В таких случаях проводится местное лечение всеми современными методами, которые есть в пульмонологии. Брахитерапия, коагуляция плазменным аргоном, лазерная терапия, криотерапия, стентирование, и их комбинация могут уменьшить симптомы сдавления дыхательных путей и избежать развития стеноза после реда осложнений, например, пневмонии (Рис 4). По этой причине пациент с раком легкого на- будуется не только онкологами, но и пульмонологами, что дает определенные преимущества.

Прогноз

В связи с тем, что большинство случаев рака легких диагностируются на стадии метастазов, прогноз остается неблагоприятным. У пациентов с метастатической стадией рака пятилетняя выживаемость составляет менее 20%.

Поскольку более 80% случаев рака легких вызваны табачным воздействием, борьба с этой вредной зависимостью может существенно сократить заболеваемость населения данным злокачественным заболеванием. Программы по профилактике табакокурения нужно проводить в школах, начиная с младших классов. Несмотря на то, что в целом проблема заболеваемости раком легкого и смертности от этого заболевания еще не решена, прогноз для отдельных пациентов и их качество жизни могут быть значительно улучшены посредством предоставления современной междисциплинарной онкологической помощи.
Diagnosis and Treatment of Morbid Obesity

Abstract

Background: Morbid obesity has become a challenging disease with growing number of affected patients. Since diagnosis and treatment of obesity can be only optimally managed in an interdisciplinary team we established the interdisciplinary platform for diagnosis and treatment of morbid obesity at the university hospital of Tübingen. Platform Adipositas: Obese patients, willing to loose weight, are seen by specialists of the endocrinologic, surgical, psychosomatic and sport medical department. In addition, patients have two appointments with special trained dietitians. Indications for bariatric surgery are discussed during the interdisciplinary conference. After surgery follow up is standardized. Patients were seen one, three, six and twelve months after surgery. After that time patients are examined on a yearly basis.

Methods: A retrospective database of 161 patients was analyzed. Of all patients, 77 underwent bariatric surgery, including 2 gastric bandings, 66 laparoscopic sleeve resections and 9 laparoscopic Roux-en-Y gastric bypasses.

Results: Mean body mass index (BMI) prior to surgery was 52.9 ± 0.9 for sleeve gastrectomy and 49.0 ± 1.8 for Roux-en-Y gastric bypass. One year after surgery mean excess weight loss (EWL) was 50.6 ± 4.0% for sleeve gastrectomy and 59.1 ± 7.0% for Roux-en-Y gastric bypass. In the sleeve gastrectomy group 7 patients (10.6%) had a port site infection and 2 (3%) patients a late staple line leakage that did not require surgical intervention. Mean volume of the resected stomach was 804 ± 35 ml with no correlation to preoperative BMI or postoperative EWL. In the Roux-en-Y gastric bypass group we had 1 (11%) patient with a port site infection. One (11%) patient with a staple line leakage and 1 (11%) with postoperative intragastric hemorrhage, respectively could be treated conservatively. There was no postoperative mortality.

Conclusions: The interdisciplinary platform for diagnosis and treatment of morbid obesity is a helpful tool in the treatment of morbid obese patients. In an interdisciplinary setting, indications for bariatric surgery have a higher quality and the interdisciplinary platform can assure a close postoperative follow up. The minor and major complications were 3 (4%) patients a staple line leakage that did not require surgical intervention, one (1%) –port site infection. In the sleeve gastrectomy group 7 patients (11%) –postoperative intragastric hemorrhage, respectively could be treated conservatively. There was no postoperative mortality.

No correlation to preoperative BMI or postoperative EWL was observed.

Mean volume of the resected stomach was 804 ± 35 ml with no correlation to preoperative BMI or postoperative EWL. In the Roux-en-Y gastric bypass group we had 1 (11%) patient with a port site infection. One (11%) patient with a staple line leakage and 1 (11%) with postoperative intragastric hemorrhage, respectively could be treated conservatively. There was no postoperative mortality.

Conclusions: The interdisciplinary platform for diagnosis and treatment of morbid obesity is a helpful tool in the treatment of morbid obese patients. In an interdisciplinary setting, indications for bariatric surgery have a higher quality and the interdisciplinary platform can assure a close postoperative follow up. The minor and major complications were 3 (4%) patients a staple line leakage that did not require surgical intervention, one (1%) –port site infection. In the sleeve gastrectomy group 7 patients (11%) –postoperative intragastric hemorrhage, respectively could be treated conservatively. There was no postoperative mortality.

No correlation to preoperative BMI or postoperative EWL was observed.
complications rate and EWL in our data is comparable with international published complication rates.

Introduction
Morbid obesity is a great challenge in modern medicine with a dramatic increasing number of patients. In European countries up to 20% of the population is obese with increasing patient numbers. Obesity is highly associated with the metabolic syndrome [1, 2], arthritis [3], sleep apnoe [4] and many other diseases. Obese women are more often infertile [5] and obesity was shown to increase the risk of unemployment [6, 7]. In a population based study performed in the United States obesity could be identified as major cause of premature mortality among middle-aged adults. Class II and III obesity increases mortality by 40% in females and 62% in males compared with normal BMI [8]. Class III obesity is difficult to treat since lifestyle intervention programs decrease body weight only by about 10 kg and long term results are quite uncertain [9, 10]. Surgery is an alternative in these patients showing very good results in terms of weight reduction [11-14], but not every patient is a candidate for surgery. To reduce surgical risks an optimal preoperative management is crucial. An interdisciplinary weight reducing program seems to be promising in long terms because of persistent lifestyle modifications for conservative and/or surgical treatment.

Material and Methods
Platform Adipositas: The platform Adipositas in Tübingen consists of the following core departments: endocrinology, sport medicine, psychosomatic, dietetics and surgery. Patients within the platform are visiting specialists of all core departments, if necessary additional examinations are made. During the first visit, patients receive a handout including all telephone numbers needed to make the necessary appointments of the departments. Patients are required to make these appointments themselves. This helps us to verify patient's compliance. After completion of the platform departments

Fig. 1: Excess weight loss after laparoscopic gastric sleeve resection. Mean follow up was 214 (26 – 1056) days. N = 66
Fig. 2: Excess weight loss after laparoscopic Roux-en-Y gastric bypass. Mean follow up was 180 (14 – 393) days. N = 9

Введение
Патологическое ожирение с постоянно увеличивающимся числом пациентов, страдающих данным заболеванием, является большой проблемой в современной медицине. В европейских странах до 20% населения страдает ожирением и их число растет. Ожирение часто сопровождается метаболическим синдромом [1, 2], артрозами [3], анапноэ во время сна [4] и многими другими заболеваниями. Тучные женщины чаще бесплодны [5], кроме того, ожирение приводит к увеличению риска безработицы [6, 7].

Популяционное исследование, проведенное в США, выявило, что ожирение является основной причиной преждевременной смертности среди взрослых людей среднего возраста. Ожирение II и III степени увеличивает смертность на 40% у женщин и 62% у мужчин по сравнению с нормальным ИМТ [8].

Ожирение III степени трудно поддается коррекции путем изменения образа жизни и системы питания, что дает уменьшение массы тела только на 10 кг, при чем долгосрочные результаты весьма неопределены [9, 10].

Альтернативное хирургическое лечение таких больных показывает очень хорошие результаты в плане снижения веса [11-14], но не каждый пациент является кандидатом для хирургического вмешательства. Для сокращения числа хирургических рисков решающее значение имеет предоперационная оценка больного. Междисциплинарные программы снижения веса представляются многообещающими в долгосрочной перспективе по причине радикальности консервативного/хирургического вмешательства.
all patients are discussed in an interdisciplinary board and therapy advices are given. Only patients with no or minimal feasibility to lose weight using conservative methods get the advice for surgery. Patients with the advice to undergo surgery need a gastroscopy in addition to general preoperative examinations prior to surgery. After weight reduction some patients need a body-contouring abdominoplasty. For these patients a plastic surgeon is associated to the platform.

Patients
Patient’s data were collected in an internal retrospective database, including 161 patients (76% female, 24% male) seen in our outpatient department from April 2010 to June 2010. Data are given as mean ± SEM.

Results
Surgery
Criteria for surgery were a positive advice in the interdisciplinary board of the platform and a positive decision of the patient’s Health insurance to cover the operation. Procedure decision was made on an expert basis.

In our database 77 patients were detected that underwent surgery since 1.1.2009, including 2 laparoscopic gastric bandings, 66 laparoscopic sleeve gastrectomies and 9 laparoscopic Roux-en-Y gastric bypass operations. The two gastric banding patients had no postoperative complications. In the sleeve gastrectomy group 7 patients (10.6%) had a port site infection and 2 patients a late staple line leakage that did not require surgical intervention. Mean volume of the resected stomach in

<table>
<thead>
<tr>
<th>Data of Patients that underwent Bariatric Surgery</th>
</tr>
</thead>
<tbody>
<tr>
<td>Patients (n)</td>
</tr>
<tr>
<td>Gastric Banding</td>
</tr>
<tr>
<td>Sleeve Gastrectomy</td>
</tr>
<tr>
<td>Roux-en-Y Gastric Bypass</td>
</tr>
</tbody>
</table>

Table 2: Data of patients that underwent bariatric surgery.
sleeve gastrectomy was 804 ± 35 ml with no correlation to preoperative body mass index (BMI) or postoperative excess weight loss (EWL). None of the patients had to be converted to an open procedure. In the Roux-en-Y gastric bypass group we had 1 (11%) patient with staple line leak that could be treated conservatively, 1 (11%) patient with a postoperative intragastric hemorrhage that did not require surgical intervention and 1 (11%) patient with postoperative port site infection. None of the patients in the laparoscopic Roux-en-Y gastrectomy group had to be converted to an open procedure. There was no postoperative mortality.

Postoperative follow up
Within the first year after surgery, follow up is usually after 4 weeks, 3 months, 6 months and 1 year. After that time patients are examined on a yearly basis. Mean follow up time for gastric sleeve resection (Fig. 1) was 214 days (range 26 – 1056 days) and for Roux-en-Y gastric bypass (Fig. 2) 180 days (range 14 – 399 days). One year after surgery patients that underwent laparoscopic sleeve gastrectomy lost 50.6 ± 4.0 % of their excess weight. Patients that underwent laparoscopic Roux-en-Y gastric bypass had an excess weight loss of 59.1 ± 7.0 % after one year.

Discussion
We present data from the platform Adipositas established at the University Hospital Tübingen, Germany. The platform Adipositas is an interdisciplinary board of specialists being responsible for diagnosis and treatment advices of obese patients willing to loose weight in the long term. We found the platform very helpful to evaluate patient’s conditions and their compliance and feasibility for conservative weight reduction. Endocrine and psychosomatic reasons for morbid obesity are closely evaluated during the platform and treated if needed. In the sport medical department constitutional capability is evaluated. The dietitians do not only inform patients about possible food changes, but they analyze food protocols together with the patients, too. All these informations are taken into account, when decision is made about surgical indications in the interdisciplinary board of the platform Adipositas.

Postoperativ follow up
Within the first year after surgery, follow up is usually after 4 weeks, 3 months, 6 months and 1 year. After that time patients are examined on a yearly basis. Mean follow up time for gastric sleeve resection (Fig. 1) was 214 days (range 26 – 1056 days) and for Roux-en-Y gastric bypass (Fig. 2) 180 days (range 14 – 399 days). One year after surgery patients that underwent laparoscopic sleeve gastrectomy lost 50.6 ± 4.0 % of their excess weight. Patients that underwent laparoscopic Roux-en-Y gastric bypass had an excess weight loss of 59.1 ± 7.0 % after one year.

Discussion
We present data from the platform Adipositas established at the University Hospital Tübingen, Germany. The platform Adipositas is an interdisciplinary board of specialists being responsible for diagnosis and treatment advices of obese patients willing to loose weight in the long term. We found the platform very helpful to evaluate patient’s conditions and their compliance and feasibility for conservative weight reduction. Endocrine and psychosomatic reasons for morbid obesity are closely evaluated during the platform and treated if needed. In the sport medical department constitutional capability is evaluated. The dietitians do not only inform patients about possible food changes, but they analyze food protocols together with the patients, too. All these informations are taken into account, when decision is made about surgical indications in the interdisciplinary board of the platform Adipositas.

Postoperativ follow up
Within the first year after surgery, follow up is usually after 4 weeks, 3 months, 6 months and 1 year. After that time patients are examined on a yearly basis. Mean follow up time for gastric sleeve resection (Fig. 1) was 214 days (range 26 – 1056 days) and for Roux-en-Y gastric bypass (Fig. 2) 180 days (range 14 – 399 days). One year after surgery patients that underwent laparoscopic sleeve gastrectomy lost 50.6 ± 4.0 % of their excess weight. Patients that underwent laparoscopic Roux-en-Y gastric bypass had an excess weight loss of 59.1 ± 7.0 % after one year.

Discussion
We present data from the platform Adipositas established at the University Hospital Tübingen, Germany. The platform Adipositas is an interdisciplinary board of specialists being responsible for diagnosis and treatment advices of obese patients willing to loose weight in the long term. We found the platform very helpful to evaluate patient’s conditions and their compliance and feasibility for conservative weight reduction. Endocrine and psychosomatic reasons for morbid obesity are closely evaluated during the platform and treated if needed. In the sport medical department constitutional capability is evaluated. The dietitians do not only inform patients about possible food changes, but they analyze food protocols together with the patients, too. All these informations are taken into account, when decision is made about surgical indications in the interdisciplinary board of the platform Adipositas.

Postoperativ follow up
Within the first year after surgery, follow up is usually after 4 weeks, 3 months, 6 months and 1 year. After that time patients are examined on a yearly basis. Mean follow up time for gastric sleeve resection (Fig. 1) was 214 days (range 26 – 1056 days) and for Roux-en-Y gastric bypass (Fig. 2) 180 days (range 14 – 399 days). One year after surgery patients that underwent laparoscopic sleeve gastrectomy lost 50.6 ± 4.0 % of their excess weight. Patients that underwent laparoscopic Roux-en-Y gastric bypass had an excess weight loss of 59.1 ± 7.0 % after one year.

Discussion
We present data from the platform Adipositas established at the University Hospital Tübingen, Germany. The platform Adipositas is an interdisciplinary board of specialists being responsible for diagnosis and treatment advices of obese patients willing to loose weight in the long term. We found the platform very helpful to evaluate patient’s conditions and their compliance and feasibility for conservative weight reduction. Endocrine and psychosomatic reasons for morbid obesity are closely evaluated during the platform and treated if needed. In the sport medical department constitutional capability is evaluated. The dietitians do not only inform patients about possible food changes, but they analyze food protocols together with the patients, too. All these informations are taken into account, when decision is made about surgical indications in the interdisciplinary board of the platform Adipositas.

Discussion
We present data from the platform Adipositas established at the University Hospital Tübingen, Germany. The platform Adipositas is an interdisciplinary board of specialists being responsible for diagnosis and treatment advices of obese patients willing to loose weight in the long term. We found the platform very helpful to evaluate patient’s conditions and their compliance and feasibility for conservative weight reduction. Endocrine and psychosomatic reasons for morbid obesity are closely evaluated during the platform and treated if needed. In the sport medical department constitutional capability is evaluated. The dietitians do not only inform patients about possible food changes, but they analyze food protocols together with the patients, too. All these informations are taken into account, when decision is made about surgical indications in the interdisciplinary board of the platform Adipositas.

Discussion
We present data from the platform Adipositas established at the University Hospital Tübingen, Germany. The platform Adipositas is an interdisciplinary board of specialists being responsible for diagnosis and treatment advices of obese patients willing to loose weight in the long term. We found the platform very helpful to evaluate patient’s conditions and their compliance and feasibility for conservative weight reduction. Endocrine and psychosomatic reasons for morbid obesity are closely evaluated during the platform and treated if needed. In the sport medical department constitutional capability is evaluated. The dietitians do not only inform patients about possible food changes, but they analyze food protocols together with the patients, too. All these informations are taken into account, when decision is made about surgical indications in the interdisciplinary board of the platform Adipositas.

Discussion
We present data from the platform Adipositas established at the University Hospital Tübingen, Germany. The platform Adipositas is an interdisciplinary board of specialists being responsible for diagnosis and treatment advices of obese patients willing to loose weight in the long term. We found the platform very helpful to evaluate patient’s conditions and their compliance and feasibility for conservative weight reduction. Endocrine and psychosomatic reasons for morbid obesity are closely evaluated during the platform and treated if needed. In the sport medical department constitutional capability is evaluated. The dietitians do not only inform patients about possible food changes, but they analyze food protocols together with the patients, too. All these informations are taken into account, when decision is made about surgical indications in the interdisciplinary board of the platform Adipositas.

Discussion
We present data from the platform Adipositas established at the University Hospital Tübingen, Germany. The platform Adipositas is an interdisciplinary board of specialists being responsible for diagnosis and treatment advices of obese patients willing to loose weight in the long term. We found the platform very helpful to evaluate patient’s conditions and their compliance and feasibility for conservative weight reduction. Endocrine and psychosomatic reasons for morbid obesity are closely evaluated during the platform and treated if needed. In the sport medical department constitutional capability is evaluated. The dietitians do not only inform patients about possible food changes, but they analyze food protocols together with the patients, too. All these informations are taken into account, when decision is made about surgical indications in the interdisciplinary board of the platform Adipositas.

Discussion
We present data from the platform Adipositas established at the University Hospital Tübingen, Germany. The platform Adipositas is an interdisciplinary board of specialists being responsible for diagnosis and treatment advices of obese patients willing to loose weight in the long term. We found the platform very helpful to evaluate patient’s conditions and their compliance and feasibility for conservative weight reduction. Endocrine and psychosomatic reasons for morbid obesity are closely evaluated during the platform and treated if needed. In the sport medical department constitutional capability is evaluated. The dietitians do not only inform patients about possible food changes, but they analyze food protocols together with the patients, too. All these informations are taken into account, when decision is made about surgical indications in the interdisciplinary board of the platform Adipositas.
has to be further evaluated. Weight reduction after sleeve gastrectomy and Roux-en-Y gastric bypass is comparable to international short term results but is lower in its tendency [14, 16-19]. One reason might be that many of our patients suffer from gonarthrosis (42%) and coxarthrosis (14%) and mean walking distance in this study was 1500 ± 299 meter. Additionally, only patients were selected for operative procedures when conservative treatment failed. Less feasibility for sports due to a high incidence of arthrosis and a supplementary negative patient selection might be responsible for slightly inferior results in terms of weight loss.

Using conservative lifestyle intervention programs for weight reduction a weight decrease of 5 to 10 kg is rational [20, 21]. In our study group mean weight prior to surgery was 146.0 ± 2.2 kg. These patients suffer very often from weight related depression and chronic arthritis as shown before. A weight reduction by 5 to 10 kg is not enough for this group of super obese patients. Surgery is right now the only reasonable therapy for this patient group.

References
Medical Professionals, Qualified Nurses and Operating Teams:

You are a medical professional or qualified and specialized nurse and looking for a new challenge in the Middle East?

You are an operating team and also interested in short-term engagements?

Please register here with your profile, your qualifications, expectations and ambitions: www.germandoctors.de

Your data will be treated with the strictest confidence and will not be disclosed to the public.

www.germandoctors.de
Modern Knee Arthroplasty

Nowadays modern knee arthroplasty offers various solutions for more and more well informed and educated patients. The authors want to serve reasonable information as different surgical treatments are not suitable for all patients’ conditions. Therefore, the aim of this article is to delight modern knee arthroplasty and explain the usage and need of unicompartmental knee arthroplasty, kinematics and ligament balancing of total knee arthroplasty as well as the need for a gender knee and a high flex knee.

Unicompartmental Knee Arthroplasty

One third of all patients with osteoarthrosis of the knee joint have solely one compartment of their knee affected. In two thirds of these cases, the patellofemoral joint is affected, in one third the medial compartment is affected, and only 3% of patients suffer from osteoarthrosis of the lateral compartment of the knee. Surgical treatment of medial osteoarthrosis of the knee joint includes high tibial osteotomy (HTO), unicompartmental knee arthroplasty (UKA) and total knee arthroplasty (TKA). This treatment is still controversially discussed because literature does not provide reliable data on outcome studies comparing HTO with UKA. Critics claim that UKAs provide inferior survival rates in comparison to TKAs and that UKAs are suitable for a small group of patients due to its limited range of indications. In addition, UKAs are known as a technically demanding procedure and should only be performed by experienced knee surgeons. A significant cut-off leading to superior clinical outcome according to the Swedish Knee Arthroplasty Register is more than 27 UKAs per year. The following benefits are discussed for UKAs. They have less morbidity in contrast to TKAs and patients need shorter rehabilitation periods. They can be implanted using a minimal invasive technique with view bone loss and good revision possibilities. Last, they provide good functional results restoring the native knee kinematics more appropriately than TKAs. Indications for implantation of an UKA have to be set strictly.
according to the following parameters: Grade and location of osteoarthritis, absence of notable retropatellar osteoarthritis, deviation of the knee axis of less than 15°, stable anterior and posterior cruciate ligament, stable medial and lateral collateral ligaments, absence of a rheumatic disease and a lateral knee compartment free of pain. A preoperative flexion of 100 degrees and extension of 10 degrees is mandatory and infected knee joints are definite contraindications for UKAs. As for TKAs the implantation can be performed with the aid of a navigation system (see Fig. 1).

**Kinematics and Ligament Balancing of Total Knee Arthroplasty**

Appropriate kinematics of total knee arthroplasty is mandatory to provide the best clinical outcome for our patients. The native knee kinematic might be altered due to different prosthetic designs and the surgeons aim should be to restore a polycentric knee axis yielding to less alteration of the knee joint. The more ligament structures (cruciate ligaments, collateral ligaments) are destroyed the more linkage is needed in prosthetic knee replacements to guarantee further stable conditions. Knee kinematics are influenced in terms of different prosthetic linkage and different types of inlays as ultra-congruent inlays or mobile bearing devices lead to different forces and surface loads on the tibial plateau. The authors believe that it is mandatory to aim at an optimal knee ligament balancing with less bone loss and possibility of revision.

И,наконец, ОКА обеспечивает хорошие функциональные результаты, более точно, чем ТКА, восстанавливая естественную кинематику колена. Показания к ОКА должны определять следующие параметры: степень и локализация остеоартрита, отсутствие выраженного ретропателлярного остеоартрита, отклонение коленной оси менее чем на 15°, стабильность передних и задних крестообразных связок, стабильность медиальных и латеральных боковых связок, отсутствие ревматического процесса, отсутствие болевого синдрома в положении латеральной экстензии (10°) является обязательными условиями для ОКА, а инфицированное колено — абсолютным противопоказанием.

Что касается ТКА, то имплантация протеза может быть выполнена с помощью навигационной системы (Рис 1).

**Fig. 1: Preoperative ap view of a medial gonarthritis and postoperative radiographs in 2 plains after implantation of a UKA with the use of a navigation system.**
Fig. 2: Preoperative ap view of a valgus-gon-arthritis and postoperative radiograph indicating a physio-logical angle.

ancing to avoid instability and inappropriate interface loads yielding to higher wear rates. Thereafter, surgeons should try to reconstruct the native knee kinematics by giving credit to a balanced medial and lateral collateral ligament as well as a balanced extension gap and flexion gap resulting in a stable midflexion of the knee joint. With a careful ligament balancing even higher varus or valgus deformations (up to 20°) can be treated with an unconstrained TKA system when combined with a necessary release of the collateral ligaments (see Fig. 2). The authors believe that the “tibia-first” operation technique is the appropriate way to restore the native knee kinematics and achieve optimal ligament balancing. Performing “tibia-first” the surgeons start with the tibial osteotomy and set the femoral osteotomies according to the ligament tension of the collateral ligaments and dorsal ligamentous structures of the knee joint.

In contrast to that, performing “femur-first” surgeons set femoral and tibial osteotomies according to the size of the prosthesis and further adapt the ligamental structures to the new kinematic situation with the use of further soft tissue release. Whilst the authors prefer “tibia-first” both techniques are equally performed by knee endoprotезировании коленного сустава для обеспечения его стабильности сустава. Кинематика колена при протезировании обусловлена посадкой эндопротеза, вкладышами различных видов (например, ультра-конгруэнтными вкладышами), а также мобильностью подшипникового устройства, которые определяют степень нагрузки на суставную поверхность большеберцовой кости.

Авторы считают, что необходимо стремиться к оптимальной балансировке связок коленного сустава, чтобы избежать нестабильности сустава и чрезмерной нагрузки на суставные поверхности, приводящие к быстрому изнашиванию.

Соответственно, хирурги должны восстановить природную кинематику коленного сустава путем сбалансированного натяжения медиальной и латеральной коллатеральных связок, а также посредством оставления надлежащего промежутка между суставными концами костей для экстензии и сгибания, в результате чего достигается стабильность коленного сустава во время сгибания.

Путем точной балансировки связок (мобилизации коллатеральных связок) во время ТКА может быть скорректирована даже выраженная варусная и вальгусная деформация (до 20°) (Рис 2). А вот, что операцион-
surgeons. Another possible way of changing the range of flexion and extension in total knee arthroplasty is a variation of the tibial slope. An increase of 1 degree of the posterior tibial slope leads to an increase of 1.7 degrees of flexion. Nevertheless, too much tibial slope might lead to less restored anterior-posterior stability and rotational stability. Thereafter, a physiological tibial slope of 5 degrees should be aimed by knee surgeons in order to provide best stability and range of motion to our patients. Another crucial point in restoring knee kinematics is the femoropatellar joint. Alterations in the femoropatellar kinematic might lead to anterior knee pain yielding 50% of all TKA revision surgeries. Therefore, the surgeons aim should be to avoid further lateralization of the patella by implanting the femoral shield in 3 degrees of external rotation and with a slightly lateral translation in order to lateralize the sulcus patellae and decrease the Q-angle. In case of fixed-bearing designs, an external rotated tibial component and lateral translation leads to a medial translation of the tuberositas tibiae and consecutively medial translation of the patellofemoral joint play. In addition, the authors recommend to resect the lateral patella facette using free hand cuts combined with a denervation leading to less anterior knee pain. These arrangements might be added by a lateral release. It is mandatory that the femoropatellar joint stays in place during flexion and extension without further adaptation at the end of the surgical procedure.

The “Gender Knee”
Two-thirds of all total knee prostheses are implanted in women. Therefore, the authors think that there is a need to discuss the development of the “gender knee” as this term might be misleading to many patients. The idea is to develop a specific prosthesis, which should be suitable for women as it might be obvious that men and women differ in terms of their anatomic conditions. Thereafter, a “gender knee” should be offered to our patients. Nevertheless these anatomic differences had to be proven as studies did not show different long-term outcome between men and women with conventional total knee prostheses. In contrast to the idea of a gender specific prosthesis, anatomical studies did not reveal significant anatomical differences between both sexes but significant differences between knee joints in general. Some

ная техника «tibia-first» («большеберцовая кость - первая») является наиболее подходящим способом восстановления природной кинематики сустава и достижения оптимальной балансировки связок. При выполнении указанной операционной техники, начинают с тибийальной остеотомии и определяют уровень феморальной остеотомии в соответствии с натяжением коллateralных связок и дорсальных связочных структур коленного сустава. При выполнении операции методом «femur-first» («бедренная кость - первая») хирурги определяют степень феморальной и тибийальной остеотомии в соответствии с размерами протеза и затем адаптируют связочный аппарат к новой кинематической ситуации, мобилизуя мягкие ткани.

Несмотря на то, что авторы отдают предпочтение технике «большеберцовая кость - первая», на практике оба метода одинаково используются хирургами. Другой возможный способ изменения амплитуды флексии и экстензии при TKA - изменение наклона голени. Увеличение наклона большеберцовой кости кзади на 1° приводит к увеличению сгибания на 1.7°.

Однако, слишком большой наклон большеберцовой кости может привести к уменьшению передне-задней и ротационной устойчивости. Поэтому целью хирурга должен стать угол наклона в 5°, который обеспечивает и устойчивость и объем движений.

Следующий важный момент в восстановлении кинематики – надколенно-бедренный сустав. Нарушения в феморо-пательной кинематике могут привести к болевому синдрому в передних отделах колена, является причиной 50% всех повторных операций после TKA. Следовательно, хирурги должны избегать бокового смешения надколенника путем имплантации бедренной поверхности при 3° внешней ротации и легкого бокового смешения с целью придания бокового направления бороздки надколенной чашечки и уменьшения Q-угла. В случае неподвижной формы эндопротеза, поверот большеберцового компонента и его боковое смещение приводит к медиальному смещению бугристости большеберцовой кости и следовательно, медиальному смещению надколенно-бедренного сустава. Кроме того, авторы рекомендуют произвести резекцию боковых фасеток надколенника в соответствии с денервацией, что приводит к уменьшению болей в передних отделах сустава. Данные манипуляции можно дополнить боковой мобилизацией. Обязательное условие: бедренно-надколенный сустав остается на месте во время сгибания-разгибания без дальнейшей адаптации в ходе операции.
patients’ femora have less width in contrast to its depth and therefore are not perfectly suitable for conventional total knee prostheses as the femoral shield might overlap. Another anatomical type for which a “gender knee” could be chosen is a small ventral overhang of the femur because the femoral shield of the “gender knee” is thinner than the one of the normal version (see Fig. 3). The gender prosthesis pays credit to these specific anatomical settings. Nevertheless, these parameters occur in both sexes, female a little more often than male patients, and therefore the authors believe that surgeons should have the possibility to implant a “gender” prosthesis in both sexes if there is an anatomical need. In addition, literature could refute the hypothesis, that women and men show different Q-angles (the angle between the tuberositas tibiae and the Quadriceps muscle) as this angle correlates with body height instead of different sexes. We believe that the gender prosthesis is one more option to come up to our patient’s individual demands. In conclusion most women do not need a specific “gender knee”. But even some men could be candidates for a “gender knee” because of their anatomical findings. Not only is the correctly chosen and implanted prosthesis mandatory for the best clinical outcome but also the individual surgeon’s experience in modern total knee arthroplasty.

Fig. 3: Preoperativ and postoperative radiograph of a 58 year old man being treated with a TKA with a gender solution. The red line on the preoperative lateral view indicates an anatomical small ventral overhang of the patient and demonstrates the need for a gender solution with a thin femoral shield to preserve a low retropatellar pressure.

Гендерное колено
Две трети всех эндопротезов имплантированы женщинам. Поэтому авторы считают, что есть необходимость обсудить целесообразность разработки и применения так называемого «гендерного эндопротеза» коленного сустава (данный термин вводит в заблуждение многих).

Идея заключается в разработке специального эндопротеза для женского колена, с учетом того, что анатомические особенности коленного сустава мужчин и женщин различаются. Поэтому, гендерный эндопротез должен быть предложен пациентам. Однако, обоснованность учета анатомических различий при протезировании должно быть доказано, так как исследования не показали разницы долгосрочных результатов обычного эндопротезирования у мужчин и женщин. В противоположность идеи гендерного эндопротезирования, специальное анатомическое исследование выявило не существенные анатомические различия женского и мужского колена, а их различия у разных индивидуумов. У некоторых пациентов бедренная кость имеет меньшую ширину, следовательно, не вполне подходит для обычного эндопротезирования, так как поверхность будет перекрыта стандартным протезом. Другим анатомический тип колена, при протезировании которого нужен гендерный протез - коленный сустав с небольшим вентральным выступом бедренной кости, так как феморальная поверхность гендерного эндопротеза тоньше, чем у его обычной версии (см. рисунок 3).
The “High Flex Knee”

Similar to the “gender” solutions high flex knee systems also seem to be a development mainly inspired by marketing since in the most studies a higher flexion compared to regular models implanted by the same surgeon could not be proven. Not the small differences in the design of the implant but proper surgical techniques are decisive for a good flexion of the patient.

The two important operative steps to improve the flexion are to increase the posterior slope of the tibial component and to remove osteophytes at the dorsal part of the femoral condyles. Especially increasing the slope must be carefully prevented to the development of an anterior-posterior instability. In general, once again the experience of the orthopedic surgeon and not the implant design is decisive for a good clinical result.

Literature


Проф. д-р Volkmar Jansson (MD)
Dr. Patrick Sadoghi (MD)
Dr. Andreas Fottner (MD)
Department for Orthopedic Surgery, University of Munich, Campus Großhadern
Volkmar.Jansson@med.uni-muenchen.de

Ordentlicher Direktor, Dr. med. Volkmar Jansson
Prof. med. Volkmar Jansson

Profiessor, doctor Volkmar Jansson
Đoktor Patick Sadoghi
Đoktor Andreas Fottner

Повышенная подвижность сустава
Как и гендерное колено, специальный эндопротез коленного сустава с повышенной подвижностью является маркетинговым моментом, поскольку большинство исследований не доказало его преимущества перед обычными моделями. Небольшие особенности в конструкции, а подходящая хирургическая техника является решающим фактором для функции сгибания. Два хирургических приема являются важными для обеспечения подвижности сустава: увеличение заднего наклона тибионального компонента и удаление остеофитов на дорсальной поверхности мышцелка бедренной кости. Основно важно увеличить наклон, чтобы предотвратить развитие передне-задней нестабильности сустава. В целом, еще раз можно повторить, что именно опыт хирурга-ортопеда, а не модель эндопротеза, имеет решающее значение для результата противоэрозирования.
Predictive Molecular Testing and Prevention of Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC, Lynch Syndrome)

Abstract
A better understanding of the molecular basis of hereditary colorectal cancer syndromes such as hereditary nonpolyposis colorectal cancer syndrome (HNPCC) yields profound consequences for the diagnosis, surveillance and prophylactic therapy of (pre)malignant neoplastic lesions. Sequence analysis of the underlying genes for these tumours and the detection of disease-causing genetic alterations in an index patient enable predictive testing for individuals at risk within an affected family. The Dresden Center for Familial Colorectal Cancer has been since 1995 active in the study of the molecular basis of several diseases, among others the HNPCC (Lynch Syndrome). Together with human geneticists and clinicians we have screened 1316 patients with hereditary tumours and performed molecular diagnostics for various syndromes such as Peutz-Jeghers Syndrome (Gene: STK11), Cowden Syndrome (PTEN), and Familial adenomatous Polyposis coli (APC, MUTYH), still the most frequent cause of familial colorectal cancer remains the HNPCC (MSH2, MLH1, MSH6 and PMS2). We have identified 224 germline mutations and performed predictive diagnostics in 296 relatives of index patients. Our prospective data on the efficacy of colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer suggest that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Key Words
HNPCC – Molecular Diagnostics – Surveillance – Treatment

Introduction
Hereditary colorectal cancer accounts for up to 5% of all colorectal cancer cases. The genetic basis for several syndromes has been elucidated, such as in the Peutz-Jeghers Syndrome (Gene: STK11), Cowden Syndrome (PTEN), Familial Juvenile Polyposis (SMAD4, BMPR1A) and Familial adenomatous Polyposis coli (APC, MUTYH). The most frequent cause of familial colorectal cancer is Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC, Lynch Syndrome), still the most frequent cause of familial colorectal cancer remains the HNPCC (MSH2, MLH1, MSH6 and PMS2). We have identified 224 germline mutations and performed predictive diagnostics in 296 relatives of index patients. Our prospective data on the efficacy of colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer suggest that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Key Words
HNPCC – Molecular Diagnostics – Surveillance – Treatment

Introduction
Hereditary colorectal cancer accounts for up to 5% of all colorectal cancer cases. The genetic basis for several syndromes has been elucidated, such as in the Peutz-Jeghers Syndrome (Gene: STK11), Cowden Syndrome (PTEN), Familial Juvenile Polyposis (SMAD4, BMPR1A) and Familial adenomatous Polyposis coli (APC, MUTYH). The most frequent cause of familial colorectal cancer is Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC, Lynch Syndrome), still the most frequent cause of familial colorectal cancer remains the HNPCC (MSH2, MLH1, MSH6 and PMS2). We have identified 224 germline mutations and performed predictive diagnostics in 296 relatives of index patients. Our prospective data on the efficacy of colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer suggest that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Key Words
HNPCC – Molecular Diagnostics – Surveillance – Treatment

Introduction
Hereditary colorectal cancer accounts for up to 5% of all colorectal cancer cases. The genetic basis for several syndromes has been elucidated, such as in the Peutz-Jeghers Syndrome (Gene: STK11), Cowden Syndrome (PTEN), Familial Juvenile Polyposis (SMAD4, BMPR1A) and Familial adenomatous Polyposis coli (APC, MUTYH). The most frequent cause of familial colorectal cancer is Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC, Lynch Syndrome), still the most frequent cause of familial colorectal cancer remains the HNPCC (MSH2, MLH1, MSH6 and PMS2). We have identified 224 germline mutations and performed predictive diagnostics in 296 relatives of index patients. Our prospective data on the efficacy of colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer suggest that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Key Words
HNPCC – Molecular Diagnostics – Surveillance – Treatment

Introduction
Hereditary colorectal cancer accounts for up to 5% of all colorectal cancer cases. The genetic basis for several syndromes has been elucidated, such as in the Peutz-Jeghers Syndrome (Gene: STK11), Cowden Syndrome (PTEN), Familial Juvenile Polyposis (SMAD4, BMPR1A) and Familial adenomatous Polyposis coli (APC, MUTYH). The most frequent cause of familial colorectal cancer is Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC, Lynch Syndrome), still the most frequent cause of familial colorectal cancer remains the HNPCC (MSH2, MLH1, MSH6 and PMS2). We have identified 224 germline mutations and performed predictive diagnostics in 296 relatives of index patients. Our prospective data on the efficacy of colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer suggest that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Key Words
HNPCC – Molecular Diagnostics – Surveillance – Treatment

Introduction
Hereditary colorectal cancer accounts for up to 5% of all colorectal cancer cases. The genetic basis for several syndromes has been elucidated, such as in the Peutz-Jeghers Syndrome (Gene: STK11), Cowden Syndrome (PTEN), Familial Juvenile Polyposis (SMAD4, BMPR1A) and Familial adenomatous Polyposis coli (APC, MUTYH). The most frequent cause of familial colorectal cancer is Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC, Lynch Syndrome), still the most frequent cause of familial colorectal cancer remains the HNPCC (MSH2, MLH1, MSH6 and PMS2). We have identified 224 germline mutations and performed predictive diagnostics in 296 relatives of index patients. Our prospective data on the efficacy of colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer suggest that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Key Words
HNPCC – Molecular Diagnostics – Surveillance – Treatment

Introduction
Hereditary colorectal cancer accounts for up to 5% of all colorectal cancer cases. The genetic basis for several syndromes has been elucidated, such as in the Peutz-Jeghers Syndrome (Gene: STK11), Cowden Syndrome (PTEN), Familial Juvenile Polyposis (SMAD4, BMPR1A) and Familial adenomatous Polyposis coli (APC, MUTYH). The most frequent cause of familial colorectal cancer is Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC, Lynch Syndrome), still the most frequent cause of familial colorectal cancer remains the HNPCC (MSH2, MLH1, MSH6 and PMS2). We have identified 224 germline mutations and performed predictive diagnostics in 296 relatives of index patients. Our prospective data on the efficacy of colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer suggest that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Key Words
HNPCC – Molecular Diagnostics – Surveillance – Treatment

Introduction
Hereditary colorectal cancer accounts for up to 5% of all colorectal cancer cases. The genetic basis for several syndromes has been elucidated, such as in the Peutz-Jeghers Syndrome (Gene: STK11), Cowden Syndrome (PTEN), Familial Juvenile Polyposis (SMAD4, BMPR1A) and Familial adenomatous Polyposis coli (APC, MUTYH). The most frequent cause of familial colorectal cancer is Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC, Lynch Syndrome), still the most frequent cause of familial colorectal cancer remains the HNPCC (MSH2, MLH1, MSH6 and PMS2). We have identified 224 germline mutations and performed predictive diagnostics in 296 relatives of index patients. Our prospective data on the efficacy of colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer suggest that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Key Words
HNPCC – Molecular Diagnostics – Surveillance – Treatment

Introduction
Hereditary colorectal cancer accounts for up to 5% of all colorectal cancer cases. The genetic basis for several syndromes has been elucidated, such as in the Peutz-Jeghers Syndrome (Gene: STK11), Cowden Syndrome (PTEN), Familial Juvenile Polyposis (SMAD4, BMPR1A) and Familial adenomatous Polyposis coli (APC, MUTYH). The most frequent cause of familial colorectal cancer is Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC, Lynch Syndrome), still the most frequent cause of familial colorectal cancer remains the HNPCC (MSH2, MLH1, MSH6 and PMS2). We have identified 224 germline mutations and performed predictive diagnostics in 296 relatives of index patients. Our prospective data on the efficacy of colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer suggest that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Key Words
HNPCC – Molecular Diagnostics – Surveillance – Treatment

Introduction
Hereditary colorectal cancer accounts for up to 5% of all colorectal cancer cases. The genetic basis for several syndromes has been elucidated, such as in the Peutz-Jeghers Syndrome (Gene: STK11), Cowden Syndrome (PTEN), Familial Juvenile Polyposis (SMAD4, BMPR1A) and Familial adenomatous Polyposis coli (APC, MUTYH). The most frequent cause of familial colorectal cancer is Hereditary Non-Polyposis Colorectal Cancer Syndrome (HNPCC, Lynch Syndrome), still the most frequent cause of familial colorectal cancer remains the HNPCC (MSH2, MLH1, MSH6 and PMS2). We have identified 224 germline mutations and performed predictive diagnostics in 296 relatives of index patients. Our prospective data on the efficacy of colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer suggest that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Key Words
HNPCC – Molecular Diagnostics – Surveillance – Treatment
Hospital Planning
following the EU guidelines

We design the future

- hospital/practice certification according to EU/ISO standards and/or KTQ certification
- planning and development of hospitals, health centres and medical practices
- hospital furnishings and infrastructure
- CT and MRI diagnosis equipment
- operating rooms and furnishings
- management structure, medical structure
- information design, interior design
- hospital and practice marketing
- presentation and appearance in public (public relations)
- internal presentation and appearance (human relations)
- development of the corporate identity (CI)
- website optimization, screen design

Hospital Engineering made in Germany
which may be responsible for 3 to 5% of all colorectal cancers. Lynch Syndrome is caused by mutations in the four mismatch repair (MMR) genes MSH2, MLH1, MSH6 and PMS2 (Lynch, 2003). Members of families with HNPCC have a higher risk for developing synchronous and metachronous tumours of the colon and rectum and the endometrium, while cancers of the stomach, ovaries, renal pelvis, ureter, biliary tract, pancreas, small bowel, brain and skin are less frequent.

On a clinical level, the identification relies on an accurate family history. HNPCC has been characterized by the “Bethesda guidelines”, revised in 2004 (Umar, 2004). To meet these guidelines, there should be a familial history of CRC or HNPCC-related cancers and/or synchronous or metachronous cancers in family members, and/or a young age at disease onset. Accordingly, the identification of the causative germline mutation in the index patient allows for predictive testing of family members at risk.

The necessity for proper assessment of the risk of familial colorectal cancer has become increasingly evident. In Germany alone, this inherited condition remains largely unrecognized in up to 3000 colorectal cancer patients per year, while the benefit of surveillance and screening in risk patients and families has been clearly documented. Further recommendations based on predictive molecular testing such as prophylactic surgical treatments, require critical evidence-based evaluation.

**The Diagnostic Procedure for the Identification of Patients with HNPCC**

The Dresden Center for Familial Colorectal Cancer has been since 1995 active in the study of the molecular basis of several diseases, among others the HNPC. In cooperation with human geneticists and clinicians, we provide counseling for patients with hereditary tumours, perform predictive molecular diagnostics in families with HNPC and recommend surveillance programs (Gebert, 1999; Plaschke, 2004; Krüger, 2005; Plaschke, 2006; Krüger, 2008).

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).

<table>
<thead>
<tr>
<th>Examinations</th>
<th>Frequency</th>
</tr>
</thead>
<tbody>
<tr>
<td>Physical examination</td>
<td>annually</td>
</tr>
<tr>
<td>Abdominal sonography</td>
<td>annually</td>
</tr>
<tr>
<td>Total colonoscopy</td>
<td>annually</td>
</tr>
<tr>
<td>Gynecological examinations for endometrial and ovarian cancer including transvaginal sonography</td>
<td>annually</td>
</tr>
<tr>
<td>Gastroscopy (starting at age 35)</td>
<td>annually</td>
</tr>
</tbody>
</table>

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).

**HNPCC**

1. A first-degree relative with HNPCC
2. A second-degree relative with HNPCC
3. An early-onset colorectal cancer in a first-degree relative
4. A synchronous or metachronous tumour, perform predictive molecular testing such as prophylactic surgical treatments
5. A hereditary nonpolyposis colorectal cancer

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).

**Colorectal Cancer**

<table>
<thead>
<tr>
<th>Physical examination</th>
<th>annually</th>
</tr>
</thead>
<tbody>
<tr>
<td>Abdominal sonography</td>
<td>annually</td>
</tr>
<tr>
<td>Total colonoscopy</td>
<td>annually</td>
</tr>
<tr>
<td>Gynecological examinations for endometrial and ovarian cancer including transvaginal sonography</td>
<td>annually</td>
</tr>
<tr>
<td>Gastroscopy (starting at age 35)</td>
<td>annually</td>
</tr>
</tbody>
</table>

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).

**HNPCC**

1. A first-degree relative with HNPCC
2. A second-degree relative with HNPCC
3. An early-onset colorectal cancer in a first-degree relative
4. A synchronous or metachronous tumour, perform predictive molecular testing such as prophylactic surgical treatments
5. A hereditary nonpolyposis colorectal cancer

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).

**Diagnosis of HNPCC**

1. A first-degree relative with HNPCC
2. A second-degree relative with HNPCC
3. An early-onset colorectal cancer in a first-degree relative
4. A synchronous or metachronous tumour, perform predictive molecular testing such as prophylactic surgical treatments
5. A hereditary nonpolyposis colorectal cancer

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).

**Treatment of HNPCC**

1. A first-degree relative with HNPCC
2. A second-degree relative with HNPCC
3. An early-onset colorectal cancer in a first-degree relative
4. A synchronous or metachronous tumour, perform predictive molecular testing such as prophylactic surgical treatments
5. A hereditary nonpolyposis colorectal cancer

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).

**Diagnosis of HNPCC**

1. A first-degree relative with HNPCC
2. A second-degree relative with HNPCC
3. An early-onset colorectal cancer in a first-degree relative
4. A synchronous or metachronous tumour, perform predictive molecular testing such as prophylactic surgical treatments
5. A hereditary nonpolyposis colorectal cancer

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).

**Diagnosis of HNPCC**

1. A first-degree relative with HNPCC
2. A second-degree relative with HNPCC
3. An early-onset colorectal cancer in a first-degree relative
4. A synchronous or metachronous tumour, perform predictive molecular testing such as prophylactic surgical treatments
5. A hereditary nonpolyposis colorectal cancer

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).

**Diagnosis of HNPCC**

1. A first-degree relative with HNPCC
2. A second-degree relative with HNPCC
3. An early-onset colorectal cancer in a first-degree relative
4. A synchronous or metachronous tumour, perform predictive molecular testing such as prophylactic surgical treatments
5. A hereditary nonpolyposis colorectal cancer

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).

**Diagnosis of HNPCC**

1. A first-degree relative with HNPCC
2. A second-degree relative with HNPCC
3. An early-onset colorectal cancer in a first-degree relative
4. A synchronous or metachronous tumour, perform predictive molecular testing such as prophylactic surgical treatments
5. A hereditary nonpolyposis colorectal cancer

The suspicion of HNPCC arises if at least one of the following five criteria of the Bethesda guidelines is met (Umar, 2004).
1. Colorectal cancer diagnosed in a patient who is less than 50 years of age.
2. Presence of synchronous, metachronous colorectal, or other HNPCC associated tumors*, regardless of age.
3. Colorectal cancer with the MSI-H histology† diagnosed in a patient who is less than 60 years of age.
4. Colorectal cancer diagnosed in one or more first-degree relatives with an HNPCC-related tumor, with one of the cancers being diagnosed under age 50 years.
5. Colorectal cancer diagnosed in two or more first- or second-degree relatives with HNPCC-related tumors, regardless of age.

(*Hereditary nonpolyposis colorectal cancer (HNPCC) related tumors include colorectal, endometrial, stomach, ovarian, pancreas, ureter and renal pelvis, biliary tract, and brain (usually glioblastoma as seen in Turcot syndrome) tumors, sebaceous gland adenomas and keratoacanthomas in Muir–Torre syndrome, and carcinoma of the small bowel.
†Presence of tumor infiltrating lymphocytes, Crohn’s-like lymphocytic reaction, mucinous/signet-ring differentiation, or medullary growth pattern.)

Consequently, tumor from the proband should be tested for mismatch repair deficiency if Bethesda guidelines are met; the proband gives written informed consent to molecular diagnostics after physician counselling. The proband is considered the affected patient through which a genetic disorder within a family is ascertained. The optimal approach to molecular evaluation is the immunohistochemical (IHC) analysis and/or microsatellite instability (MSI) testing of the proband tumor, aiming to identify the knocked-out mismatch repair (MMR) gene (Engel, 2006). More than 50% of probands meeting Bethesda guidelines do not exhibit MMR deficiencies within the tumour, hence sequence analysis of one of the four mismatch repair genes is not recommended in these cases. Immunohistochemical analysis of the tumor preceeds germline testing of one or two of the four MMR genes (MLH1, MSH2, MSH6 or PMS2), in accordance to the expression levels of each protein in the tumour. After mutation detection, the index patient is informed during.

Fig. 1: Predictive molecular diagnostics in HNPCC

<table>
<thead>
<tr>
<th>164 index persons</th>
<th>258 family members</th>
</tr>
</thead>
<tbody>
<tr>
<td>164 HNPCC</td>
<td>31 HNPCC</td>
</tr>
<tr>
<td>101 mutation carriers</td>
<td>126 family members without mutation</td>
</tr>
</tbody>
</table>

296 mutation carriers
HNPPCC-surveillance recommended

126 family members without mutation
HNPPCC-surveillance required

Подозрение на ННКР возникает, если пациент соответствует хотя бы одному из следующих пяти критериев Bethesda (Umar, 2004):
1. Колоректальный рак (КР) диагностирован у пациента моложе 50 лет
2. Наличие синхронных, метахронных опухолей толстой кишки, или других опухолей, связанных с ННКР, независимо от возраста.
3. Наличие у пациента моложе 60 лет с диагнозом КР типичной для MSI-H гистологии.
4. Пациент любого возраста с колоректальным раком, имеющий родственника первой степени с КР или опухолями, связанными с ННКР, (Одна из опухолей должна была быть диагностирована раньше 50 года жизни.)
5. Наличие у пациента с КР не менее двух родственников первой или второй степени с КР или опухолями заболеваниями, связанными с ННКР, независимо от их возраста.

(Опухоли, связанные с наследственным неполипозным колоректальным раком (ННКР), включают рак прямой кишки, эндометрия, желудка, яичников, поджелудочной железы, мочеточника и почечной лоханки, желчевыводящих путей, (синдром Turcot), опухоли сальных желез и аденомы, кератокантомы, синдром Muir-Torre и рак тонкой кишки.

Иммуногистохимический анализ опухоли предваряет генеративное исследование одного или двух из четырех генов MMR MLH1, MSH2, MSH6 или PMS2 в зависимости от уровня протеинов в опухоли. Пациент будет проинформирован о выявленных мутациях в ходе генетического консультирования. При выявленной мутации род-
ing genetic counselling. Relatives should then be referred for genetic counselling and predictive genetic testing. A HNPCC specific surveillance is highly recommended for persons fulfilling one of the following criteria:

1. The proband meets Bethesda guidelines, the tumor is MMR deficient and no MMR gene mutation has been found.
2. The person is a relative of the proband (see 1.)
3. The person carries a pathogenic germline mutation in one of the four MMR genes.

Surveillance is recommended starting at the age of 25, or 5 years before the age of diagnosis in the youngest family member (see Table 1).

Results from Molecular Diagnostics and Surveillance of HNPCC Patients

At the Dresden Center for Familial Colorectal Cancer we have offered counselling and molecular diagnostics to 1316 patients. 1058 patients were index patients and 258 patients underwent predictive diagnostics. 935 index patients met the Bethesda criteria and 351 patients presented with a MMR defect. We identified 164 pathogenic germline mutations in MLH1 (76), MSH2 (59), MSH6 (20) and PMS2 (9). In addition, we found 60 unclassified variants. We performed predictive diagnostics in 258 relatives of index persons and identified the mutation in 132 relatives for whom we recommended the annual surveillance program (Fig. 1).

Recently, the German HNPCC Consortium including our Centre at Dresden published prospective data on the efficacy of annual colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer (Engel, 2010). We found a good compliance to annual examinations, with 81% of colonoscopies completed within 15 months. Ninety-nine CRC events were observed in 90 patients. Seventeen CRCs (17%) were detected through symptoms (8 before baseline colonoscopy, 8 at intervals more than 15 months to the preceding colonoscopy, and 1 interval cancer). Only 2 of 43 CRCs detected by follow-up colonoscopy were regionally advanced. Tumor stages were significantly lower among CRCs detected by follow-up colonoscopies compared with CRCs detected through clinical symptoms. We conclude that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Conclusions

We identified 351 patients presented with a MMR defect. We met the Bethesda criteria and the diagnosis in 132 relatives for whom we recommended the annual surveillance program (Fig. 1).

We have offered genetic counselling and predictive genetic testing. A HNPCC specific surveillance is highly recommended for persons fulfilling one of the following criteria:

1. The proband meets Bethesda guidelines, the tumor is MMR deficient and no MMR gene mutation has been found.
2. The person is a relative of the proband (see 1.)
3. The person carries a pathogenic germline mutation in one of the four MMR genes.

Surveillance is recommended starting at the age of 25, or 5 years before the age of diagnosis in the youngest family member (see Table 1).

Results from Molecular Diagnostics and Surveillance of HNPCC Patients

At the Dresden Center for Familial Colorectal Cancer we have offered counselling and molecular diagnostics to 1316 patients. 1058 patients were index patients and 258 patients underwent predictive diagnostics. 935 index patients met the Bethesda criteria and 351 patients presented with a MMR defect. We identified 164 pathogenic germline mutations in MLH1 (76), MSH2 (59), MSH6 (20) and PMS2 (9). In addition, we found 60 unclassified variants. We performed predictive diagnostics in 258 relatives of index persons and identified the mutation in 132 relatives for whom we recommended the annual surveillance program (Fig. 1).

Recently, the German HNPCC Consortium including our Centre at Dresden published prospective data on the efficacy of annual colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer (Engel, 2010). We found a good compliance to annual examinations, with 81% of colonoscopies completed within 15 months. Ninety-nine CRC events were observed in 90 patients. Seventeen CRCs (17%) were detected through symptoms (8 before baseline colonoscopy, 8 at intervals more than 15 months to the preceding colonoscopy, and 1 interval cancer). Only 2 of 43 CRCs detected by follow-up colonoscopy were regionally advanced. Tumor stages were significantly lower among CRCs detected by follow-up colonoscopies compared with CRCs detected through clinical symptoms. We conclude that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Conclusions

We identified 351 patients presented with a MMR defect. We met the Bethesda criteria and the diagnosis in 132 relatives for whom we recommended the annual surveillance program (Fig. 1).

We have offered genetic counselling and predictive genetic testing. A HNPCC specific surveillance is highly recommended for persons fulfilling one of the following criteria:

1. The proband meets Bethesda guidelines, the tumor is MMR deficient and no MMR gene mutation has been found.
2. The person is a relative of the proband (see 1.)
3. The person carries a pathogenic germline mutation in one of the four MMR genes.

Surveillance is recommended starting at the age of 25, or 5 years before the age of diagnosis in the youngest family member (see Table 1).

Results from Molecular Diagnostics and Surveillance of HNPCC Patients

At the Dresden Center for Familial Colorectal Cancer we have offered counselling and molecular diagnostics to 1316 patients. 1058 patients were index patients and 258 patients underwent predictive diagnostics. 935 index patients met the Bethesda criteria and 351 patients presented with a MMR defect. We identified 164 pathogenic germline mutations in MLH1 (76), MSH2 (59), MSH6 (20) and PMS2 (9). In addition, we found 60 unclassified variants. We performed predictive diagnostics in 258 relatives of index persons and identified the mutation in 132 relatives for whom we recommended the annual surveillance program (Fig. 1).

Recently, the German HNPCC Consortium including our Centre at Dresden published prospective data on the efficacy of annual colonoscopic surveillance in individuals with hereditary nonpolyposis colorectal cancer (Engel, 2010). We found a good compliance to annual examinations, with 81% of colonoscopies completed within 15 months. Ninety-nine CRC events were observed in 90 patients. Seventeen CRCs (17%) were detected through symptoms (8 before baseline colonoscopy, 8 at intervals more than 15 months to the preceding colonoscopy, and 1 interval cancer). Only 2 of 43 CRCs detected by follow-up colonoscopy were regionally advanced. Tumor stages were significantly lower among CRCs detected by follow-up colonoscopies compared with CRCs detected through clinical symptoms. We conclude that annual colonoscopic surveillance is recommended for individuals with HNPCC.

Conclusions

We identified 351 patients presented with a MMR defect. We met the Bethesda criteria and the diagnosis in 132 relatives for whom we recommended the annual surveillance program (Fig. 1).

We have offered genetic counselling and predictive genetic testing. A HNPCC specific surveillance is highly recommended for persons fulfilling one of the following criteria:

1. The proband meets Bethesda guidelines, the tumor is MMR deficient and no MMR gene mutation has been found.
2. The person is a relative of the proband (see 1.)
3. The person carries a pathogenic germline mutation in one of the four MMR genes.

Surveillance is recommended starting at the age of 25, or 5 years before the age of diagnosis in the youngest family member (see Table 1).
Conclusions
Bethesda guidelines, microsatellite analysis and immunohistochemistry are important diagnostic tools for identification of HNPCC patients who are likely to carry pathogenic germline mutations in mismatch repair genes. Sequence analyses of MMR genes in our patients with MMR-deficient tumors identified germline mutations in 64% of patients. Predictive molecular diagnostics was offered to 258 family members. Annual colonoscopic surveillance is recommended for individuals with HNPCC.

Acknowledgement: We appreciate the translation into Russian by Roman Bannack.

References


Vыводы
Критерии Bethesda, микросателлитный анализ (MSA) и иммуногистохимия (ICH) являются важными диагностическими инструментами для выявления пациентов с наследственным полипозным колоректальным раком (ННПКР, синдромом Линча), которые чаще всего являются носителями патогенных мутаций генов репарации, отвечающих за систему репарации. Последующее исследование MMR геном у пациентов с MMR-дефектной мутацией важно для выявления генеративных мутаций у 64% пациентов. Предиктивная молекулярная диагностика была предложена 258 родственникам. При наличии ННПКР рекомендуется ежегодное колоноскопическое исследование.

Примечание: Благодарим Романа Баннак за помощь при переводе статьи на русский язык.
**Transcatheter Valve Therapies**

**Introduction**

In recent years, transcatheter aortic valve implantation (TAVI) has become clinical routine in patients with severe symptomatic aortic stenosis (AS). While TAVI is currently restricted to high-risk patients and surgical aortic valve replacement (AVR) remains the reference treatment, a broader clinical application of TAVI can be anticipated in the future.

Non-surgical intervention for treatment of mitral regurgitation (MR) is a second field of intense investigation. Here, the growing incidence of congestive heart failure has created an unmet clinical need of less invasive treatment strategies especially for patients with functional MR.

This article summarizes the current state of transcatheter aortic and mitral valve interventions and discusses future perspectives.

**Key words:** Transcatheter, percutaneous, aortic valve replacement, mitral valve repair, aortic stenosis, mitral regurgitation

---

**Transcatheter Aortic Valve Implantation**

**Background and Patient Selection**

The overwhelming majority of aortic valve interventions is performed due to degenerative disease with its clinical manifestation as calcified AS. For this entity, surgical AVR is currently the treatment of choice with well defined indications [1] and low perioperative morbidity and mortality [2]. Even in an elderly population with relevant comorbidities, surgical AVR can be carried out with good patient outcomes [3,4,5].

It is however a clinical reality that a substantial share of patients meeting the formal criteria for AVR are deemed inoperable due to real or presumed contraindications to surgery. A recent analysis of the Euro Heart Survey found that one-third of all patients with severe symptomatic AS are not referred to surgery, mostly because of advanced age or left ventricular (LV) dysfunction [6]. The dismal prognosis of medically treated AS on the other hand has triggered the development of less invasive, non-surgical intervention for treatment of mitral regurgitation (MR) is a second field of intense investigation. Here, the growing incidence of congestive heart failure has created an unmet clinical need of less invasive treatment strategies especially for patients with functional MR.

This article summarizes the current state of transcatheter aortic and mitral valve interventions and discusses future perspectives.

**Key words:** Transcatheter, percutaneous, aortic valve replacement, mitral valve repair, aortic stenosis, mitral regurgitation
beating-heart, catheter-based techniques for aortic valve implantation. Multiple technical and procedural refinements have led to the clinical introduction of different devices, two of which, the Edwards Sapien™ valve (Edwards Lifesciences Inc., USA) and the CoreValve™ system (Medtronic Inc., USA), have received commercial approval in Europe (CE mark).

Today most clinicians involved agree that TAVI should be restricted to patients deemed inoperable due to comorbidities. These comorbidities include severe calcifications of the ascending aorta (“porcelain aorta”), end-stage organ failure of lung, liver or kidneys, a history of coronary surgery with patent grafts or a history of chest radiation. Risk stratification tools such as the logistic EuroSCORE (>20%) or the Society of Thoracic Surgeons (STS) score (>10%) may also be helpful in determining the individual treatment strategy. Both transfemoral and transapical AVI can only be executed successfully if performed as an interdisciplinary team approach involving cardiologists, cardiac surgeons, anesthesiologists and radiologists with their respective specialized expertise.

**Transcatheter Aortic Valve Implantation – Current and Future Devices**

**The Edwards Sapien Valve**
The Edwards Sapien valve consists of a balloon-expandable stainless-steel stent surrounded by a sealing cuff made of polyester fabric, in which a trileaflet valve of bovine pericardium is mounted.

The valve is crimped onto a balloon delivery catheter prior to implantation and is deployed by balloon expansion under rapid ventricular pacing.

**The CoreValve Prosthesis**
In contrast to the Edwards Sapien valve, the CoreValve prosthesis is of a self-expanding design. The leaflets are constructed from porcine pericardium and are mounted inside a tubular nitinol mesh frame with allows for compression at low temperatures and resumes its original form when released at body temperature. Because the implant is self-expanding and immediately compatible,
petent, repeated rapid pacing is not necessary for valve deployment. With the 3rd generation device, both valves can now be implanted through a delivery sheath measuring only 18F which permits a purely percutaneous procedure in selected cases without the need for surgical cut-down (Fig. 1).

**The Direct Flow Valve**

Continuing problems of the aforementioned devices in terms of paravalvular leakage and the inability to reposition or even retrieve valves after final deployment have led to the development of the Direct Flow™ device (Direct Flow Medical Inc., USA; Fig. 2). The Direct Flow prosthesis is a stentless valve type consisting of bovine pericardium which is suspended in a conformable polyester fabric cuff and designed for transfemoral implantation.

The “first-in-man” application was performed by our group with encouraging results both acutely and at 6-month follow-up [7, 8].

Among the many other devices currently under development, some have been evaluated in pre-clinical or early clinical trials (Fig. 3).

**Techniques of Transcatheter Aortic Valve Implantation**

Today, two approaches for TAVI are being routinely used: a retrograde transfemoral approach via puncture or surgical cut-down of the femoral artery [9] (Fig. 4) or an antegrade transapical approach via a left anterolateral mini-thoracotomy [10, 11].

At present, there is no scientific proof of superiority of one technique over the other. Many groups consider the completely closed-chest transfemoral approach as the technique of first choice and resort to the transapical approach only in cases of contraindications (e.g., severe peripheral artery disease) which may make femoral vascular access impossible. Severe tortuosity of the abdominal aorta (passage) or a heavily calcified aortic arch (stroke risk) also must be taken into account.

In clinical practice, the optimal strategy must be carefully planned according to the individual patient’s characteristics.

**Протез клапана CoreValve Prosthesis**

В отличие от клапана Edwards Sapien, протез клапана CoreValve имеет самораскрывающуюся конструкцию. Створки сделаны из свиного перикарда и установлены внутри цилиндрической нитиноевой сетчатой рамки, которая сжимается при низкой температуре и принимает обычный размер при температуре тела. Поскольку имплантат является самораскрывающимся и сразу же рабочим, не нужна повторная стимуляция для его расправления. С помощью устройств 3-го поколения клапаны теперь могут быть имплантированы путем чисто чрескожной процедуры без необходимости хирургического вмешательства (рис. 1).

**Прямоточный клапан Direct Flow Valve**

Ряд проблем при применении ранее упомянутых клапанов — подтекание через клапаны, невозможность переместить и удалить клапан после его полного расправления, привело к разработке устройства Direct FlowTM (Direct Flow Medical Inc., USA; Рис 2). Протез Direct Flow — бесстенотический клапан, сделанный из бычьего перикарда, который помещен в мягкую полиэстеровую манжетку и сконструирован для трансфеморальной имплантации. Первое применение его “на людях” было осуществлено нашей группой с обнадеживающими результатами сразу после процедуры и после 6 месяцев наблюдения [7, 8].

Среди других разработанных клапанов, некоторые уже прошли доклинические испытания и ранние клинические испытания (рис. 3).

**Техника транскатетерной имплантации аортального клапана**

В настоящее время в клинической практике используются два метода TAVI: посредством ретроградного трансфеморального доступа посредством феморальной артерии / разреза феморальной артерии [9] (Рис. 4) или путем использования антеградного трансапикального доступа посредством передней мини-торакотомии слева. [10, 11]. В настоящее время нет никаких научных доказательств превосходства одного метода над другим.

Многие группы считают трансфеморальный подход методом выбора и прибегают к трансапикальному только в случаях...
Both types of procedure are ideally performed in a specially equipped hybrid operating suite, providing the implanting personnel with adequate technical equipment should emergency conversion to surgery with cardiopulmonary bypass become necessary. Modern imaging techniques are essential to guide the implantation process. The combination of transesophageal echocardiography (TEE), fluoroscopy and aortic angiography guarantees optimal conditions for TAVI.

Results after Transcatheter Aortic Valve Implantation

After TAVI, substantial improvement in the patient’s functional capacity was observed within the first month. Functional improvements were most pronounced in patients who were in New York Heart Association (NYHA) class III and IV at baseline and who improved by at least one functional class. When reporting results after TAVI, the pronounced risk profile of the treated patient population must be taken into account. Generally, patients are in their eighties and are afflicted with severe comorbidities making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.

A recent review on the safety of TAVI procedures summarizes patient outcomes excluding early series, where a procedural learning curve is expected to impact early results [12]. The authors found 30-day mortality rates to range between 6.4 to 7.4% and 11.6 to 18.6% in the transfemoral and transapical series, respectively. Table 1 provides an overview of the most recent series at leading heart centers in this field.

Many groups report a tendency towards more adverse events and higher mortality rates in patients treated by transapical TAVI as opposed to the transfemoral approach. However, detailed analysis of the respective patient populations has revealed patient risk factors to be responsible for this effect rather than procedural determinants making them unfit as surgical candidates. Their logistic EuroSCORE (event though known to overestimate procedural risk) usually ranges between 20 and 30%. Furthermore, TAVI is a relatively young technique with a steep learning curve.
In a transfemoral-first approach to TAVI as advocated by most groups, patient selection will lead to patients with more severe comorbidities in the transapical groups. Learning curve remains one of the most important predictors of procedural success and mortality. From the older Registry of Endovascular Implantation of Valves in Europe (REVIVE) to the more recent Edwards Sapien™ Aortic Bioprosthesis European Outcome (SOURCE) registry every new study conducted in this field revealed higher success rates and lower mortality rates with increasing experience.

Transcatheter Mitral Valve Repair

Background

Surgical mitral valve repair (MVR) strategies have evolved with constant technical refinements ever since the underlying mechanisms were classified in the landmark paper “The French Correction” by Alain Carpentier in 1983 [15]. Differentiation of the complex pathophysiology of MR is beyond the scope of this article. However, in addressing modern therapy for MR, it is most important to distinguish between primary (organic) and secondary (functional) MR. In primary MR, dysfunction of the valve itself leads to regurgitation and subsequent volume overload of the LV. If this condition persists long enough, it will lead to LV remodeling and dysfunction. Since there is a definite causal relation between primary MR and its effects on the LV, surgical correction of the defect, preferably MVR, is usually curative.

In contrast, secondary MR is rather the consequence of ventricular dysfunction caused by coronary artery disease or other causes of “dilated cardiomyopathy”. Therefore, in this entity, the benefit of restoring MV function is less certain.

Surgical correction of secondary MR by the use of restrictive annuloplasty has proven to induce reverse remodeling and a modest improvement in LV function [16]. However, as of yet, there is no proof that such interventions lead to improved patient survival [17, 18]. It is for this growing patient population that non-surgical means for the modern therapy for MR, it is most important to distinguish between primary (organic) and secondary (functional) MR. In primary MR, dysfunction of the valve itself leads to regurgitation and subsequent volume overload of the LV. If this condition persists long enough, it will lead to LV remodeling and dysfunction. Since there is a definite causal relation between primary MR and its effects on the LV, surgical correction of the defect, preferably MVR, is usually curative.

In contrast, secondary MR is rather the consequence of ventricular dysfunction caused by coronary artery disease or other causes of “dilated cardiomyopathy”. Therefore, in this entity, the benefit of restoring MV function is less certain.

Surgical correction of secondary MR by the use of restrictive annuloplasty has proven to induce reverse remodeling and a modest improvement in LV function [16]. However, as of yet, there is no proof that such interventions lead to improved patient survival [17, 18]. It is for this growing patient population that non-surgical means for the modern therapy for MR, it is most important to distinguish between primary (organic) and secondary (functional) MR. In primary MR, dysfunction of the valve itself leads to regurgitation and subsequent volume overload of the LV. If this condition persists long enough, it will lead to LV remodeling and dysfunction. Since there is a definite causal relation between primary MR and its effects on the LV, surgical correction of the defect, preferably MVR, is usually curative.

In contrast, secondary MR is rather the consequence of ventricular dysfunction caused by coronary artery disease or other causes of “dilated cardiomyopathy”. Therefore, in this entity, the benefit of restoring MV function is less certain.

Surgical correction of secondary MR by the use of restrictive annuloplasty has proven to induce reverse remodeling and a modest improvement in LV function [16]. However, as of yet, there is no proof that such interventions lead to improved patient survival [17, 18]. It is for this growing patient population that non-surgical means for the modern therapy for MR, it is most important to distinguish between primary (organic) and secondary (functional) MR. In primary MR, dysfunction of the valve itself leads to regurgitation and subsequent volume overload of the LV. If this condition persists long enough, it will lead to LV remodeling and dysfunction. Since there is a definite causal relation between primary MR and its effects on the LV, surgical correction of the defect, preferably MVR, is usually curative.

In contrast, secondary MR is rather the consequence of ventricular dysfunction caused by coronary artery disease or other causes of “dilated cardiomyopathy”. Therefore, in this entity, the benefit of restoring MV function is less certain.

Surgical correction of secondary MR by the use of restrictive annuloplasty has proven to induce reverse remodeling and a modest improvement in LV function [16]. However, as of yet, there is no proof that such interventions lead to improved patient survival [17, 18]. It is for this growing patient population that non-surgical means for the modern therapy for MR, it is most important to distinguish between primary (organic) and secondary (functional) MR. In primary MR, dysfunction of the valve itself leads to regurgitation and subsequent volume overload of the LV. If this condition persists long enough, it will lead to LV remodeling and dysfunction. Since there is a definite causal relation between primary MR and its effects on the LV, surgical correction of the defect, preferably MVR, is usually curative.

In contrast, secondary MR is rather the consequence of ventricular dysfunction caused by coronary artery disease or other causes of “dilated cardiomyopathy”. Therefore, in this entity, the benefit of restoring MV function is less certain.

Surgical correction of secondary MR by the use of restrictive annuloplasty has proven to induce reverse remodeling and a modest improvement in LV function [16]. However, as of yet, there is no proof that such interventions lead to improved patient survival [17, 18]. It is for this growing patient population that non-surgical means for the modern therapy for MR, it is most important to distinguish between primary (organic) and secondary (functional) MR. In primary MR, dysfunction of the valve itself leads to regurgitation and subsequent volume overload of the LV. If this condition persists long enough, it will lead to LV remodeling and dysfunction. Since there is a definite causal relation between primary MR and its effects on the LV, surgical correction of the defect, preferably MVR, is usually curative.
treatment of secondary MR, which often occurs in the wake of congestive heart failure, seem most promising.

In recent years, a multitude of transcatheter approaches for the treatment of MR has been developed, some of which attempt to emulate established surgical techniques. Transcatheter techniques of MVR include coronary sinus (CS) annuloplasty, direct annuloplasty, leaflet repair strategies and LV chamber remodeling devices. This review will focus on the CS annuloplasty and leaflet repair techniques since it is with these devices that most clinical experience has been gathered to date.

**Coronary Sinus Annuloplasty Devices**

One of the cornerstones of modern surgical MVR is the use of annuloplasty rings either alone or in addition to valvuloplasty techniques. In order to downsize mitral annular dimensions or stabilize additional repair procedures, the ring must be firmly anchored in the mitral annulus, especially at the two fibrous trigones. Anatomical studies have revealed the distance between the CS and the fibrous trigones to reach up to several centimeters, allowing for a commissure-to-commissure at best [19].

Also, the anterior aspect of the mitral annulus is not addressed and may be subject to further dilatation in heart failure patients. Another issue is the fact that in healthy hearts the CS courses at a distance of 5.8 to 14 mm from the mitral annulus [20]. This distance has been shown to increase even further in patients with dilatation of the LV and mitral annulus [21]. Finally, concern has been expressed regarding a possible interposition of the left circumflex artery between the CS and the mitral annulus, which has been reported to be present in up to 80% of hearts investigated [20]. It may be for these reasons that results after CS

<table>
<thead>
<tr>
<th>Institution</th>
<th>Reference no.</th>
<th>Valve type</th>
<th>TF / TA approach</th>
<th>Number patients (n)</th>
<th>logEuro SCORE (%)</th>
<th>30d mortal. (%)</th>
<th>Stroke (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Siegburg</td>
<td>Grube JACC 2007</td>
<td>CV</td>
<td>TF</td>
<td>86</td>
<td>21.5</td>
<td>12</td>
<td>10</td>
</tr>
<tr>
<td>Vancouver</td>
<td>Webb Circ 2007</td>
<td>ES</td>
<td>TF</td>
<td>50</td>
<td>28</td>
<td>12</td>
<td>4</td>
</tr>
<tr>
<td>Leipzig</td>
<td>Walther Thorac Cardiovasc Surg 2010</td>
<td>ES</td>
<td>TA</td>
<td>240</td>
<td>32.0</td>
<td>9.5</td>
<td>0.8</td>
</tr>
<tr>
<td>Munich</td>
<td>Bleiziffer EJCTS 2009</td>
<td>CV / ES</td>
<td>TA / TF</td>
<td>137</td>
<td>24.3</td>
<td>12.4</td>
<td>5.1</td>
</tr>
<tr>
<td>Hamburg</td>
<td>Seiffert Thorac Cardiovasc Surg 2010</td>
<td>ES</td>
<td>TA / TF</td>
<td>116</td>
<td>27.1</td>
<td>12.9</td>
<td>5.2</td>
</tr>
</tbody>
</table>

**Table 1: Results after TF- and TA-AVI at selected leading heart centers**

Таблица 1: Результаты после TF- и TA-AVI в отдельных ведущих кардиохирургических центрах сердца

**Results after TF- and TA-AVI at Selected Leading Heart Centers**

Именно для этой растущей популяции пациентов, нехирургические методы лечения вторичной MR, которая появляется как результат застойной сердечной недостаточности, кажутся наиболее перспективными. За последние годы было разработано множество транскатетерных методов лечения MR, некоторые из которых «симвулировали» уже имеющиеся хирургические методы.

Транскатетерные методы MVR включают: аннулопластику коронарного синуса (КС), прямую аннулопластику, пластiku створок клапана (реконструкция митрального клапана по типу «край-в-край», заплатка из перикарда, мобилизация створок, восстановление хорд), ремонтолевирование камеры левого желудочка.

Данный обзор посвящен аннулопластике КС и методу пластик створок клапана поскольку по ним собран наибольший на сегодняшний день клинический опыт.

**Устройство для аннулопластики коронарного синуса**

Одним из краеугольных камней современной хирургической MVR
Percutaneous Leaflet Repair
In the surgical literature, an edge-to-edge MVR technique has been described by Ottavio Alfieri and colleagues in 2001 [24] whereby the edges of the anterior (AML) and the posterior (PML) mitral leaflets are sewn together at the coaptation line, producing a double-orifice valve. Today, the Alfieri technique is primarily indicated in primary MR due to AML prolapse or, in selected cases, bileaflet prolapse. Attempts to emulate this surgical maneuver by catheter-based techniques have been pursued.

Device and Procedure
The MitraClip® system (Abbott, USA) consists of a steerable guiding catheter, a clip delivery system, and the MitraClip device (Fig. 6). The MitraClip is composed of a cobalt-chromium alloy covered with polyester fabric to promote progressive endothelial encapsulation. The clip has two arms corresponding to each leaflet, and each arm is paired with a gripper with frictional elements. Leaflets are secured between the arm and the gripper. The system is introduced via the right femoral vein. Transseptal access is achieved in the standard fashion but is facilitated and more precise with transesophageal echocardiography guidance. The 24-F guiding catheter is advanced from the groin through the septum over a stiff wire. The clip delivery system is advanced through the guide into the left atrium and then steered into a position coaxial with the long axis of the LV over the MR jet. The open clip arms are aligned perpendicular to the line of

approaches to MR have been widely disappointing.

To date, relevant clinical experience has been reported with three CS devices.

The Monarc device (Edwards Lifesciences, Fig. 5a) was tested in the EVOLUTION-I feasibility and safety trial. Successful device implantation was reported in 82% (59/72 patients) and a significant reduction in MR severity in the majority of patients. However, 30-day MACE rate was 9% (death, myocardial infarction, cardiac tamponade) and there was evidence of coronary compression in more than 25% (15/59) of all cases.

Results from the prospective multi-center AMADEUS trial (CArillon Mitral Annuloplasty Device European Union Study) using the Carillon™ device (Cardiac Dimensions Inc, USA; Fig. 5b) have recently been published [22]. Successful device implantation was achieved in 30 of 48 patients (60%). In over 30% of patients, the device had to be recaptured due to various reasons (coronary compromise, insufficient reduction of MR, device failure). Overall MACE rate was 14.6% at 30 days and included death, myocardial infarction and CS perforation/dissection.

A third device, the Percutaneous Transvenous Mitral Annuloplasty (PTMA) system (Viacor Inc., USA) was tested in a preliminary safety study (PTOLEMY I-trial) [23], while proof of functional benefit regarding MR reduction is still pending (PTOLEMY II-trial).
leaflet coaptation. The clip is then advanced into the LV and slowly withdrawn to the level of the leaflets. The leaflet-grasping technique has evolved such that the clip is pulled back slowly, allowing the leaflets to fall onto the clip arms. The grippers are then lowered, and the arms are partially closed to capture the leaflets. Once a secure leaflet grasp with adequate leaflet tissue between the arms and the gripper has been confirmed, the clip is fully closed for further coaptation of the leaflets, and the resulting reduction in MR severity is assessed (Fig. 7, 8). A second clip may be placed if more leaflet coaptation is required for a broader MR jet origin.

Clinical Experience
The MitraClip has been evaluated in a phase 1 clinical trial (EVEREST I) and in the ongoing EVEREST II trial. To qualify for treatment, patients had to have a clinical indication for mitral valve surgery with at least grade 3+ MR.

The EVEREST I study was a phase 1 registry to evaluate safety. EVEREST II is the pivotal study randomizing standard surgical risk patients in a 2:1 fashion to MitraClip or open surgical repair or replacement, respectively.

Results from the initial 107 patients treated in EVEREST I and II (roll in) have been reported [25]. This initial cohort of patients had a mixture of pathologies, with 79% degenerative and 21% functional etiology. Although acute procedural success was defined in the protocol as a reduction of baseline MR grade to ≤ 2+, the goal of the procedure was to reduce MR to trace or maximally grade 1+ and to maintain the acutely achieved MR reduction in the long-term. Of this cohort of 107 patients, 74% had discharge MR grade ≤ 2+, 10% were aborted without clip implantation due to inability to adequately reduce MR, and 16% had a clip implantation but discharge MR grade was rated > 2+. Thus, procedural outcomes were acceptable given the learning curves of the operators, with a 30-day free-
dom of major adverse events rate of 91%. The majority of patients with adequate MR reduction at 30 days have sustained MR reduction out to 12 months, regardless of etiology. Mean length of hospitalization was low at 3.2 days. Clinical benefit was evident through sustained improvement in NYHA functional class at 1 year for patients with adequate procedural MR reduction.

Recently, Ted Feldman presented the results of the Endovascular Valve Edge-to-Edge REpair Study (EVEREST II) randomized clinical study as a late breaking clinical trial at the American College of Cardiology 59th Annual Scientific Sessions (March 14, 2010). In this study, 279 patients were enrolled at 37 clinical sites; 184 patients were treated with the MitraClip device, whereas the control group of 95 patients was treated by surgical repair or valve replacement. Patients were included if they were candidates for mitral valve surgery with moderate-to-severe (3+) or severe (4+) MR. The demographic data were comparable between both groups.

The primary endpoints were safety (major adverse event rate at 30 days) and effectiveness (clinical success rate). The results can be summarized in brief as follows. The safety endpoint was 9.6% for the MitraClip device patients and 57% for the mitral valve surgery patients. The clinical success rate at 12 months was 72% for the MitraClip device patients and 88% for the mitral valve surgery patients.

Therefore, clinical benefit was demonstrated for the MitraClip system and mitral valve surgery patients out to 12 months. For both groups, an improved LV function, improved NYHA functional class, and improved quality of life was demonstrated. Furthermore, the authors stated that when needed, mitral valve surgery remains a viable option following the MitraClip procedure.

From these data one might conclude that, given the safety, effectiveness, and clinical benefits, the MitraClip procedure is an important therapeutic option for selected high-risk patients with significant MR.

**Clinical Experience**

The device MitraClip was evaluated in the EVEREST II clinical trial. The results of the randomized clinical study (EVEREST I and II) as a late-breaking clinical trial at the American College of Cardiology 59th Annual Scientific Sessions (March 14, 2010). In this study, 279 patients were enrolled at 37 clinical sites; 184 patients were treated with the MitraClip device, whereas the control group of 95 patients was treated by surgical repair or valve replacement. Patients were included if they were candidates for mitral valve surgery with moderate-to-severe (3+) or severe (4+) MR. The demographic data were comparable between both groups.

The primary endpoints were safety (major adverse event rate at 30 days) and effectiveness (clinical success rate). The results can be summarized in brief as follows. The safety endpoint was 2.6% for the MitraClip device patients and 57% for the mitral valve surgery patients. The clinical success rate at 12 months was 72% for the MitraClip device patients and 88% for the mitral valve surgery patients.

Therefore, clinical benefit was demonstrated for the MitraClip system and mitral valve surgery patients out to 12 months. For both groups, an improved LV function, improved NYHA functional class, and improved quality of life was demonstrated. Furthermore, the authors stated that when needed, mitral valve surgery remains a viable option following the MitraClip procedure.

From these data one might conclude that, given the safety, effectiveness, and clinical benefits, the MitraClip procedure is an important therapeutic option for selected high-risk patients with significant MR.

**Clinical Study**

The device MitraClip was evaluated in the EVEREST II clinical trial. The results of the randomized clinical study (EVEREST I and II) as a late-breaking clinical trial at the American College of Cardiology 59th Annual Scientific Sessions (March 14, 2010). In this study, 279 patients were enrolled at 37 clinical sites; 184 patients were treated with the MitraClip device, whereas the control group of 95 patients was treated by surgical repair or valve replacement. Patients were included if they were candidates for mitral valve surgery with moderate-to-severe (3+) or severe (4+) MR. The demographic data were comparable between both groups.

The primary endpoints were safety (major adverse event rate at 30 days) and effectiveness (clinical success rate). The results can be summarized in brief as follows. The safety endpoint was 9.6% for the MitraClip device patients and 57% for the mitral valve surgery patients. The clinical success rate at 12 months was 72% for the MitraClip device patients and 88% for the mitral valve surgery patients.

Therefore, clinical benefit was demonstrated for the MitraClip system and mitral valve surgery patients out to 12 months. For both groups, an improved LV function, improved NYHA functional class, and improved quality of life was demonstrated. Furthermore, the authors stated that when needed, mitral valve surgery remains a viable option following the MitraClip procedure.

From these data one might conclude that, given the safety, effectiveness, and clinical benefits, the MitraClip procedure is an important therapeutic option for selected high-risk patients with significant MR.

The primary endpoints were safety (major adverse event rate at 30 days) and effectiveness (clinical success rate). The results can be summarized in brief as follows. The safety endpoint was 9.6% for the MitraClip device patients and 57% for the mitral valve surgery patients. The clinical success rate at 12 months was 72% for the MitraClip device patients and 88% for the mitral valve surgery patients.

Therefore, clinical benefit was demonstrated for the MitraClip system and mitral valve surgery patients out to 12 months. For both groups, an improved LV function, improved NYHA functional class, and improved quality of life was demonstrated. Furthermore, the authors stated that when needed, mitral valve surgery remains a viable option following the MitraClip procedure.

From these data one might conclude that, given the safety, effectiveness, and clinical benefits, the MitraClip procedure is an important therapeutic option for selected high-risk patients with significant MR.

**Clinical Experience**

The device MitraClip was evaluated in the EVEREST II clinical trial. The results of the randomized clinical study (EVEREST I and II) as a late-breaking clinical trial at the American College of Cardiology 59th Annual Scientific Sessions (March 14, 2010). In this study, 279 patients were enrolled at 37 clinical sites; 184 patients were treated with the MitraClip device, whereas the control group of 95 patients was treated by surgical repair or valve replacement. Patients were included if they were candidates for mitral valve surgery with moderate-to-severe (3+) or severe (4+) MR. The demographic data were comparable between both groups.

The primary endpoints were safety (major adverse event rate at 30 days) and effectiveness (clinical success rate). The results can be summarized in brief as follows. The safety endpoint was 9.6% for the MitraClip device patients and 57% for the mitral valve surgery patients. The clinical success rate at 12 months was 72% for the MitraClip device patients and 88% for the mitral valve surgery patients.

Therefore, clinical benefit was demonstrated for the MitraClip system and mitral valve surgery patients out to 12 months. For both groups, an improved LV function, improved NYHA functional class, and improved quality of life was demonstrated. Furthermore, the authors stated that when needed, mitral valve surgery remains a viable option following the MitraClip procedure.

From these data one might conclude that, given the safety, effectiveness, and clinical benefits, the MitraClip procedure is an important therapeutic option for selected high-risk patients with significant MR.

The primary endpoints were safety (major adverse event rate at 30 days) and effectiveness (clinical success rate). The results can be summarized in brief as follows. The safety endpoint was 9.6% for the MitraClip device patients and 57% for the mitral valve surgery patients. The clinical success rate at 12 months was 72% for the MitraClip device patients and 88% for the mitral valve surgery patients.

Therefore, clinical benefit was demonstrated for the MitraClip system and mitral valve surgery patients out to 12 months. For both groups, an improved LV function, improved NYHA functional class, and improved quality of life was demonstrated. Furthermore, the authors stated that when needed, mitral valve surgery remains a viable option following the MitraClip procedure.

From these data one might conclude that, given the safety, effectiveness, and clinical benefits, the MitraClip procedure is an important therapeutic option for selected high-risk patients with significant MR.

The primary endpoints were safety (major adverse event rate at 30 days) and effectiveness (clinical success rate). The results can be summarized in brief as follows. The safety endpoint was 9.6% for the MitraClip device patients and 57% for the mitral valve surgery patients. The clinical success rate at 12 months was 72% for the MitraClip device patients and 88% for the mitral valve surgery patients.

Therefore, clinical benefit was demonstrated for the MitraClip system and mitral valve surgery patients out to 12 months. For both groups, an improved LV function, improved NYHA functional class, and improved quality of life was demonstrated. Furthermore, the authors stated that when needed, mitral valve surgery remains a viable option following the MitraClip procedure.

From these data one might conclude that, given the safety, effectiveness, and clinical benefits, the MitraClip procedure is an important therapeutic option for selected high-risk patients with significant MR.

The primary endpoints were safety (major adverse event rate at 30 days) and effectiveness (clinical success rate). The results can be summarized in brief as follows. The safety endpoint was 9.6% for the MitraClip device patients and 57% for the mitral valve surgery patients. The clinical success rate at 12 months was 72% for the MitraClip device patients and 88% for the mitral valve surgery patients.

Therefore, clinical benefit was demonstrated for the MitraClip system and mitral valve surgery patients out to 12 months. For both groups, an improved LV function, improved NYHA functional class, and improved quality of life was demonstrated. Furthermore, the authors stated that when needed, mitral valve surgery remains a viable option following the MitraClip procedure.

From these data one might conclude that, given the safety, effectiveness, and clinical benefits, the MitraClip procedure is an important therapeutic option for selected high-risk patients with significant MR.

The primary endpoints were safety (major adverse event rate at 30 days) and effectiveness (clinical success rate). The results can be summarized in brief as follows. The safety endpoint was 9.6% for the MitraClip device patients and 57% for the mitral valve surgery patients. The clinical success rate at 12 months was 72% for the MitraClip device patients and 88% for the mitral valve surgery patients.

Therefore, clinical benefit was demonstrated for the MitraClip system and mitral valve surgery patients out to 12 months. For both groups, an improved LV function, improved NYHA functional class, and improved quality of life was demonstrated. Furthermore, the authors stated that when needed, mitral valve surgery remains a viable option following the MitraClip procedure.

From these data one might conclude that, given the safety, effectiveness, and clinical benefits, the MitraClip procedure is an important therapeutic option for selected high-risk patients with significant MR.
Functional MR can be defined as MR in the absence of leaflet pathology. This is generally related to leaflet tethering in ischemic disease from previous myocardial infarction or papillary muscle displacement and annular enlargement with poor leaflet coaptation in non-ischemic dilated cardiomyopathy. Surgical results for functional MR have generally been less favorable compared to those with degenerative disease, mostly related to residual or recurrent MR within the first year [26]. Thus, the functional MR patient population is an important subgroup, in which new technologies such as the MitraClip have a potential to become a viable treatment alternative.

As of today, our group has gathered the largest single-center experience with the MitraClip system worldwide with well over 120 patients treated. The majority of those patients had functional MR.

The device was exclusively being applied in patients with severe comorbidities and a prohibitively high surgical risk as evaluated by an interdisciplinary team of cardiologists and cardiac surgeons. Usually, these patients presented with functional MR or mixed MV disease (MR grade 3+ or 4+ in all patients) in combination with cardiomyopathy. In an interim analysis, outcome after treatment of 51 patients was assessed [27]. Mean patient age was 72 ± 9 years; mean LV ejection fraction was 36 ± 17%. Risk stratification revealed a mean logistic EuroSCORE of 29 ± 22%. Clip implantation was successful in 96.1% (49/51 patients). Most patients were treated by a single clip, while 2 clips were used in 14 patients (28.5%), and 3 clips were used in 2 patients (4.1%). Despite pronounced risk profile, there were no major periprocedural complications and no in-hospital mortality. At discharge, severity of MR was reduced by one grade in 16 patients (32.7%), by two grades in 24 patients (48.9%) and by three grades in 9 patients (18.4%). Whether these favorable acute results will translate into long-term benefit will have to be awaited. Preliminary

In this study, 279 patients on 37 clinical bases; 184 patients underwent mitral valve surgery (Mitral Valve Repair or Replacement) in 95 patients who underwent MitraClip, with a mean logistic EuroSCORE of 29 ± 22%. Clip implantation was successful in 96.1% (49/51 patients). Most patients were treated by a single clip, while 2 clips were used in 14 patients (28.5%), and 3 clips were used in 2 patients (4.1%). Despite pronounced risk profile, there were no major periprocedural complications and no in-hospital mortality. At discharge, severity of MR was reduced by one grade in 16 patients (32.7%), by two grades in 24 patients (48.9%) and by three grades in 9 patients (18.4%). Whether these favorable acute results will translate into long-term benefit will have to be awaited. Preliminary
experience seems to suggest relevant reduction of MR in the majority of patients and marked clinical improvement regarding NYHA functional class at 3 months of follow-up (own unpublished data).

Future Perspectives

In view of an aging population and a rising prevalence of valvular heart disease, transcatheter heart valve therapies will gain increasing weight in the future. At present, technical deficiencies and unknown long-term performance of current-generation devices limit their clinical application for a broader patient population. Modern valve surgery has evolved over decades to become the standard of care for the vast majority of patients with excellent clinical outcome.

For TAVI, current technical problems seem resolvable and an extension of the technique to younger and healthier patients appears likely. However, before expanding inclusion criteria, randomized clinical trials are needed to compare TAVI to surgical AVR and to determine the adequate treatment strategy for the individual patient. At present, we believe that evaluation of patients for TAVI or surgery is best accomplished by a dedicated interdisciplinary team of cardiologists and cardiac surgeons at specialized heart centers. For the future, randomized controlled trials are needed to further determine the role of TAVI. Therefore, the currently ongoing North American PARTNER Trial (Placement of AoRTic TranScatheter Valve Trial) is randomizing high-risk patients to transfemoral or transapical TAVI using the Edwards Sapien™ valve or to the standard of care (surgical AVR or medical therapy); results are expected in 2013.

Regarding MV disease, the bar for transcatheter therapy may be even higher. For degenerative disease, where surgical strategies are highly complex procedures comprising combined valvuloplasty and annuloplasty in most cases, it seems most unlikely that any interventional technique will ever be able to compete. Functional MR on the other hand, may represent a new indication for palliative transcatheter treatment with clips in combination with resection of the MV leaflets. The results from the PARTNER Trial show that the Edwards Sapien™ valve provides a functional improvement in 76% of patients with severe MR after TAVI [24].

Surgical therapy is usually recommended for severe MR in cases of degenerative disease, for instance mitral annular calcification, and patients with myxomatous degeneration of the mitral valve. Mitral valve repair is considered the gold standard of treatment for symptomatic MV disease, with success rates of up to 90%. However, in case of severe MR, the surgical success rate is reported to be lower, with a significant risk of complications such as atrial fibrillation [25].

Fig. 8: 3D echo with the delivery catheter advanced through the interatrial septum, with clip still attached after grasping of MV leaflets (a). Final angiographic result after deployment of two clips (b).
ment as an adjunct to medical therapy in otherwise inoperable patients.

References


В будущем, необходимы рандомизированные клинические испытания для уточнения роли TAVI в кардиохирургической практике. Так, проводимое в настоящее время североамериканское испытание PARTNER Trial (Placement of AoRTic Transcatheter Valve Trial) рандомизирует пациентов с высоким риском для трансфеморальной и трансапикальной TAVI с использованием клапана Edwards Sapien™ или стандартного лечения (хирургического или миокардиохирургического) и результаты ожидается в 2013 году.

При заболеваниях митрального клапана, потребность в транскатетерной терапии может быть еще выше. При левочервенных заболеваниях, где хирургические методы являются очень сложными и дорогостоящими, в последнее время появляется возможность применения TAVI. Перспективы на будущее при заболеваниях митрального клапана свидетельствуют о том, что TAVI может стать новым стандартом лечения для подавляющего большинства пациентов с митральным пороком.

Современная хирургия клапанов сердца развивалась на протяжении десятилетий, чтобы стать стандартом лечения для подавляющего большинства пациентов с клиническим результатом.

Для TAVI, текущие технические проблемы кажутся разрешимыми, и более широкое применение данной техники у более молодых и здоровых пациентов представляется достаточно вероятным. Однако, до расширения пока- заний, необходимо проведение рандомизированных клинических испытаний для сравнения TAVI и хирургической пластике клапанов целью определения адекватной стратегии лечения для конкретного пациента.

Мы считаем, что оценка паци- ентов для TAVI или операции лучше всего достигается путем специальной междисциплинарной команды кардиологов и кардио- хирургов в специализированных кардиологических центрах.
Change of Paradigm in Dental Local Anesthesia

Alternatives to IANB and Infiltration Anesthesia

Local anesthesia – a permanent problem in dental practice – has made considerable progress since the last Status report: the periodontal ligament injection, presented by J.A. Giovannitti and T.A. Nique and published in the JADA 1983; 106: 222-224 (11). The authors came to the conclusion, that the periodontal ligament injection technique or intraligamentary anesthesia is an effective means of producing adequate pulpal anesthesia for dental procedures. The specially adapted syringes available at that time: pistol-type syringes such as Ligmaject and Peripress offered the advantage – compared to conventional syringes – of standardizing the dose (0.2 ml per trigger pull) and to assist the dentist in delivering the high pressure necessary for the success of the technique – state of the art at that time. The authors did not recommend routine use of the technique of intraligamentary injections because of extreme operator variability and the potential for postinjection complications, due to the armamentarium available at that time and the lack of scientific evaluation of this anesthesia method.

Scientific Progress
In 1983 the need of additional research was defined by GIOVANNITI and NIQUE to determine
• The histologic effects on the periodontal ligament produced by the special periodontal ligament syringes
• The spread of the anesthetic solution through the periodontal ligament and adjacent structures
• The mechanism of anesthetic action
• The effects of this injection on the dental pulp tissue.

WALTON and GARNICK (25) (1982) who used standard syringes for the periodontal ligament injection to evaluate the histologic effects on the periodontium in monkeys, came to the conclusion that the procedure is safe to the periodontium. FUHS et al. (7) (1983) – using pistol-type syringes Peripress to inject into the periodontal ligament in dogs – and GALILI et al. (8) (1984) – using a Peripress syringe – found that the procedure is safe to the periodontium. However, they did not recommend routine use of this technique because of extreme operator variability and the potential for postinjection complications. The authors did not recommend routine use of the technique of intraligamentary injections because of extreme operator variability and the potential for postinjection complications, due to the armamentarium available at that time and the lack of scientific evaluation of this anesthesia method.
The spread of the anesthetic solution through the periodontal ligament and adjacent structures was investigated first by GaRFUnKeL et al. (9) in 1983 and at almost the same time by SMiTH and WaLTon (21) as well as by PLaGMann and JaGenoW (20) (1984).

The use of radiopaque material permitted GARFUNKEL et al. to follow the spread of the injected material through the dental tissues. It was found that the radiopaque material injected under pressure (with a Peripress syringe) filled the bone marrow spaces at the alveolar crest area of the interdental septum and advanced apically through the bone, avoiding the PDL. Maxillary and mandibular teeth, both anterior and posterior, in the two monkeys all showed an identical radiological picture. The intraligamentary anesthesia approach produced its effect through spreading an intraosseous path.

Radiopaque solutions and colloidal dyes were injected in dogs singly and in combination, distribution was determined radiographically and visually. As in clinical practice, SMiTH and WALTON – using a standard aspirating syringe equipped with a 25-gauge short needle – made the attempt to give the injections under pressure. The material was therefore presumably forced out into the tissues and was not undergoing diffusion. Examination of the spread of the injected anesthetic agent is intra-osseous.

Risunok 1: Распространение введенного анестетика внутри кости

Garfunkel was found to spread into the bone marrow and bone matrix, and not be confined to the periodontal ligament. 

Fig. 1: The spread of the injected anesthetic agent is intra-osseous.
The effect of anesthesia itself depends very much on the anesthetic solution administered. The question “Periodontal ligament injection: with or without a vasoconstrictor?” has been treated and answered convincingly by Gray, Lomax and Rood (13) (1987). A study was undertaken to directly compare the success rate for achieving analgesia using lignocaine 2% with adrenaline (epinephrine) 1:80,000 and plain lignocaine 2% when administered via the periodontal ligament. There was a 91.6% success rate when using 2% lignocaine with 1:80,000 adrenaline, whereas the success rate with 2% plain lignocaine was only 42%.

The effects of periodontal ligament injection on the dental pulp tissue were evaluated in a histological study by Lin, Lapeyrolerie, Skribner and Shovlin (17) published in 1985. This study was undertaken to histologically evaluate the effects of a periodontal ligament injection of local lignocaine was only 42%.

Repeated injections at the same site, however, tear desmodontal fibers from the alveolar-bone.

These answers to the question of the spread of the anesthetic solution also dispose of the lack of information regarding the mechanism of anesthetic action:

The anesthetic solution injected into the periodontal ligament space is diffusing via the desmodontal tissues into the spongy alveolar bone. Thus the anesthetic reaches the nerve endings surrounding the tooth and – around 30 seconds after injection – the apex and the apical foramen, producing the required analgesia without latency.

The question “Periodontal ligament injection: with or without a vasoconstrictor?” has been treated and answered convincingly by Gray, Lomax and Rood (13) (1987). A study was undertaken to directly compare the success rate for achieving analgesia using lignocaine 2% with adrenaline (epinephrine) 1:80,000 and plain lignocaine 2% when administered via the periodontal ligament. There was a 91.6% success rate when using 2% lignocaine with 1:80,000 adrenaline, whereas the success rate with 2% plain lignocaine was only 42%.

The effects of periodontal ligament injection on the dental pulp tissue were evaluated in a histological study by Lin, Lapeyrolerie, Skribner and Shovlin (17) published in 1985. This study was undertaken to histologically evaluate the effects of a periodontal ligament injection of local lignocaine was only 42%.
WHAT ABOUT YOUR BRANDING FOR YOUR INTERNATIONAL STANDING?

IS YOUR ADVERTISING FIT FOR THE WORLDWIDE PLATFORM OF THE 21ST CENTURY?

Linea Nova
advanced communication
Ruffinistraße 16
D-80637 München
Telefon +49/(0)89/57 87 57 89
Telefax +49/(0)89/13 16 30
eMail info@linea-nova.com
Internet www.linea-nova.com

Branding / Corporate Design
Webdesign
3D-Artwork / Media Design
anesthetic containing various concentrations of epinephrine on pulp tissue. Intraligamental injections of 2% lidocaine (lignocaine) with 1:100,000 and 1:50,000 epinephrine were administered to the canine and molar teeth of cats. The animals were killed at 0, 30 and 60 minutes and at 1, 3 and 7 days after injection. Histological examination showed that no pathological changes in the pulp occurred in any of the experimental teeth. The conclusions were:

1. No pathological changes, such as hydric degeneration, ischemic necrosis, or inflammation, were observed in the pulps of any experimental teeth.
2. Evidence of irreversible damage to the periodontal ligament was not present.
3. Periodontal ligament injection of 2% lidocaine with 1:50,000 epinephrine may be used for endodontic therapy in medically uncompromised patients.

Whether the PDL may be used for health compromised patients was subject of a study by GARFUNKEL, KAUFMAN and GALILI (10) published in 1985: Intraligamentary anesthesia (transligamentary anesthesia) for medically compromised patients.

The authors write that the hazards of local anesthesia for health compromised patients led to the development of the intraligamentary method. 69 patients including “bleeders” and cardiovascular cases were included in the study. 0.2 – 0.8 ml anesthetic solution was injected.

No signs of epinephrine-induced cardiac rate changes were reported by the patients or recorded by the dentist. No bleeding or hematomas were observed. There were no cases of syncope or loss of consciousness.

The depth of local anesthesia was satisfactory. The degree of anesthesia achieved was satisfactory and similar to the results obtained in healthy patients.

1. Pathological changes, such as, hydric degeneration, ischemic necrosis or watery swelling were not observed in any of the experimental teeth. The conclusions were:
2. Evidence of irreversible damage to the periodontal ligament was not present.
3. Periodontal ligament injection of 2% lidocaine with 1:50,000 epinephrine may be used for endodontic therapy in medically uncompromised patients.

Whether the PDL may be used for health compromised patients was subject of a study by GARFUNKEL, KAUFMAN and GALILI (10) published in 1985: Intraligamentary anesthesia (transligamentary anesthesia) for medically compromised patients.

Table 2: With regard to dolor post extractionem there are no significant differences.

<table>
<thead>
<tr>
<th>Wound healing Disturbances</th>
<th>Intraligamentary anesthesia = ILA</th>
<th>IANB</th>
<th>Infiltration anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Number of patients</td>
<td>83</td>
<td>85</td>
<td>87</td>
</tr>
<tr>
<td>Number of teeth extracted = N</td>
<td>110</td>
<td>110</td>
<td>110</td>
</tr>
<tr>
<td>Maxilla</td>
<td>N 56 = 50.9 %</td>
<td>N 76  = 69.1 %</td>
<td></td>
</tr>
<tr>
<td>Mandible</td>
<td>N 54 = 49.1 %</td>
<td>N 110 = 100 %</td>
<td>N 34 = 30.1 %</td>
</tr>
<tr>
<td>Dolor post extractionem</td>
<td>6 cases</td>
<td>5 cases</td>
<td>3 cases</td>
</tr>
</tbody>
</table>

**Anesthesia:**

- Need of completion: N 15 = 13.6 % N 17 = 15.5 % N 29 = 26.4 %
- Average quantity injected: 0.3 ml 2.4 ml 2.6 ml
- Injection latency time*: Practically none – 3 min – 2 min
- Duration of anesthesia*: 30 min – 3 hours – 2.5 hours
- Injection pain*: N 8 = 7.2 % N 11 = 10 % N 22 = 20 %

*| information by patient Origin: R.Heizmann, Berlin: Diss.1987

And Galili (10) (результаты были опубликованы в 1985 году): Интралигаментарная анестезия у пациентов с отягощенным анамнезом.

Авторы пишут, что опасность обычной местной анестезии для здоровья пациентов с отягощенным анамнезом привело к развитию метода интралигаментарного введения анестетика. 69 пациентов, в том числе, с повышенной кровоточивостью и сердечно-сосудистыми заболеваниями, были включены в исследование. Вводилось 0,2-0,8 ml анестезирующего раствора.

Ни каких признаков адреналин-индуктированного изменения сердечной деятельности у пациентов не было отмечено. Также не наблюдалось кровотечения или гематомы. Не было случаев обморока. Степень местной анестезии была удовлетворительной. Степень полученной анестезии было удовлетворительной и аналогичной результатам, получены у здоровых пациентов.

Группа из 69 пациентов включала: 26 пациентов с геморрагическим диатезом, 13 пациентов с сердечно-сосудистыми заболеваниями, 4 пациентов, получающих стероидную терапию, 3 пациентов на гемодиализе, 3 больных, получающих химиотерапию, 5 пациентов с талассемией, 10 больных с неврологическими расстройствами, 5 – с другими
A group of 69 patients was included in the study: 26 bleeding diathesis patients, 13 cardiovascular disease patients, 4 patients on chronic steroid therapy, 3 hemodialysis patients, 3 patients on chemotherapy, 5 thalassemia patients, 10 neurological disorders patients, 5 miscellaneous. The injections were administered with the Peripress-syringe; the anesthetic used was 2.0% lidocaine (lignocaine) with epinephrine 1:100,000, the amount of anesthetic administered varied between 0.2 – 0.8 ml, depending on the tooth to be anesthetized.

The method seems to be reliable, simple and with no side-effects and as such is recommended for patients with health compromising conditions. Most of the problems encountered by the dentist while injecting local anesthetics to health compromised patients can be avoided by the use of the intraligamentary-transligamentary approach (GA RFUnKeL, KA UF Man and Ga Li Li (10) 1985).

The special aspects of the use of intraligamental injections in hemophiliacs were studied by STOLL and BÜHRMANN (22) (1983) and by AH PIN (1) (1987). They state that hemorrhage and hematoma due to needle trauma of the conventional nerve block anesthesia can be excluded by using the intraligamentary anesthesia. They evaluated 236 extractions and achieved an anesthesia success rate of 90.26 % after the first injection and further 5.93 % after a second intraligamental injection. They came to the conclusion that this method of anesthesia is an enrichment regarding pain elimination for extraction treatment of patients with bleeding disorders.

The aspect of wound healing disturbances after extraction of teeth (dry socket, dolor post extractionem, localized

заболеваниями.Инъекции проводились шприцем Peripress; в качестве анестетика использовали 2,0% лидокаина (лигнокаина) с адреналином 1:100,000, количество анестетика колебалось от 0,2 до 0,8 мл, в зависимости от размера зуба, который нужно было анестезировать.

Метод представляется надежным, простым и без побочных эффектов, и поэтому рекомендуется для пациентов с различными заболеваниями. Большинство проблем, с которыми сталкиваются стоматологи при введении местных анестетиков пациентам с сопутствующими заболеваниями, можно избежать путем использования интралигаментарного

метода. (Garfunkel, Kaufman и Galili (10) 1985).

Аспекты использования ИЛА у больных с гемофилией изучались STOLL и BÜHRMANN (22) (1983) и AH PIN (1) (1987). Они отметили, что кровоизлияния и гематомы вследствие травмы от иглы при обычной анестезии могут быть исключены с помощью интралигаментарной анестезии. Они оценили 236 экстракций зубов: показатель успешности анестезии составил 90,26% после первой инъекции и 5,93% после второй интралигаментарной инъекции. Они пришли к выводу, что этот метод анестезии является большим достижением в области обезболивания при удалении зубов у пациентов с нарушениями свертываемости крови.

Вопросы нарушения заживления ран после экстрагирования зубов (сухая лунка, болевой синдром, альвеолярный остиг) были изучены Heizmann и Gabka (14) (1994). Впервые метод ИЛА сравнили с страдиционными методами местной стоматологической анестезии: проводной (блокадой нижнего альвеолярного нерва) и инфильтрационной анестезией. Что касается такого симптома, как болевой синдром, то не было представлено достоверных данных, чтобы оценить статистическую вероятность методом Chi-square analysis. Также
alveolar osteitis) was treated by HEIZMANN and GABKA (14) (1994). For the first time the intraligamentary anesthesia was compared in a published study to the conventional methods of local dental anesthesia: inferior alveolar nerve block and infiltration anesthesia.

With regard to wound healing disturbances (dolor post extractions) diagnosed, no significance is given to assessing a statistical probability according to the Chi-square analysis.

The authors comment that the infection is not solely provoked by the injection but by the apical osteitis of the destroyed tooth (see Table 2).

Also of concern is the sepsis that might result from forcing bacteria into the tissues and into the bloodstream (bacteremia) with the needle. WALTON and ABBOTT (24) (1981) summarized that this presumably does occur, but probably to no greater extent than with other dental procedures. The periodontal ligament injection might be compared with subgingival scaling, which has been shown to result in a bacteremia in a small percentage of cases; this bacteremia was transient. However, it must be emphasized in this connection that particular caution must be observed in the case of endocarditis-prone patients because an intrusion of bacteria from the blood may lead to serious complications for the patient. In particular, invasive operations under anti-biotic protection must be carried out (FRENKEL (6) 1989, ZUGAL (28) 2005). GLOCKMANN and TAUBENHEIM (2002) (12) define that the risk of endocarditis is an absolute contraindication for the ILA.

Unwanted side effects and impairments after the end of an intraligamentary anesthesia mentioned in the literature (FAULKNER (5) 1983, KAUFMANN et al. (16) 1983, MALAMED (18) 1982) such as discomfort or elongation feeling very often have their origin in an injection of the anesthetic solution not sufficiently taking into consideration the individual anatomic structure of the patient. HUBER and WILHELM-HÖFT (15) (1988) have shown in their study that teeth can be moved in their alveolus.

In the course of the injection (into the periodontal ligament) a volume of liquid is pressed into a space that is already completely filled. Since liquids are incompressible, an extension of the alveolar socket or a shifting of the periodontal authors pointed out that infection was provoked not only by the injection, but also by apical osteitis of the destroyed tooth (see Table 2).

Table 3: The injection pressure necessary to overcome the tissue back-pressure is reducing with the increase of the injection time.

<table>
<thead>
<tr>
<th>Injection system</th>
<th>Injection time for 0.2 ml per injection</th>
</tr>
</thead>
<tbody>
<tr>
<td>SoftJect</td>
<td></td>
</tr>
<tr>
<td>0.3 mm injection needle</td>
<td>10 s</td>
</tr>
<tr>
<td>Minimum pressure</td>
<td>0.23</td>
</tr>
<tr>
<td>Maximum pressure</td>
<td>0.06</td>
</tr>
</tbody>
</table>

The injection pressure can be calculated as follows:

- Minimum pressure: 0.06 MPa
- Maximum pressure: 0.23 MPa

The injection pressure for 0.2 ml per injection is summarized in Table 3.

Table 3: The injection pressure necessary to overcome the tissue back-pressure is reducing with the increase of the injection time.
liquid buffer may be caused in the case of a too rapid injection, in the way of a hydraulic pressure compensation effect. To avoid the unwanted effects, the anesthetic solution has to be administered very slowly, permitting the tissue to resorb the quantity of anesthetic agent injected.

**Medico-Technical Progress**

Most recent studies and evaluations of an important number of clinical data show that the success of the intraligamentary anesthesia and the absence of unwanted effects depend on an awareness of the mechanism of the method, the capability of the operator to practice the periodontal ligament injection in the state of the art and the use of appropriate materials.

WALTON and ABBOTTs (24) study in 1981 examined the periodontal ligament injection by using standard syringes. MALAMED (18) (1982) compared conventional syringes with the – at that time – new syringes of the pistol-type Peripress and Ligmaject. The results obtained with these new syringes were slightly superior to those reached with the conventional syringes (see Fig. 2).

For all studies cited – except HEIZMANN and GABKA (14) (1994) – the operators used pistol-type syringes. HEIZMANN and GABKA used syringes of the dosing-lever-type. These syringes are supplying a smaller quantity of 0.06 ml per depression of the dosing lever, instead of 0.2 ml per trigger-movement of the pistol-type syringes; the operator variability and the potential for postinjection complications being thus reduced. Nevertheless, even these PDL-syringes allowed the dentist to force the injection and to create unwanted effects – result of the “lever” system (see Fig. 3).

As a consequence a syringe type without a “lever” was developed: instead a “wheel” aided the operator during his administering of the anesthetic solution and allowed him to adapt the applied force – necessary to overcome the back-pressure of the periodontal tissue – precisely to the individual anatomic situation of the patient.

TOBIEN and SCHULZ (23) (2000) checked in an examination at fresh pig jaws whether the injection pressure can be adapted with this novel syringe to the anatomical structure in such a way that undesired effects can be avoided. The measured values show that the time factor has a considerable

Walton and Abbott in (24) investigated in 1981 that injections with periapical ligaments were superior to those reached with new syringes. Malamed (18) (1982) compared ordinary syringes with, at that time, new syringes – Peripress and Ligmaject. Results, obtained with the use of new syringes, were somewhat higher, especially when comparing the results of conventional syringes of the pistol-type SoftJect and Gabka (14) (1994), the operators used pistol-type syringes.

Tobien and Schulz (23) (2000) proved on swine that the use of new syringes can reduce the complications after the injection in comparison with conventional syringes. Tobien and Schulz used syringes of the dosing-lever-type. Heizmann and Gabka (1994) compared conventional syringes with the – at that time – new syringes of the pistol-type Peripress and Ligmaject. The results obtained with these new syringes were slightly superior to those reached with the conventional syringes (see Fig. 2).

For all studies cited – except HEIZMANN and GABKA (14) (1994) – the operators used pistol-type syringes. HEIZMANN and GABKA used syringes of the dosing-lever-type. These syringes are supplying a smaller quantity of 0.06 ml per depression of the dosing lever, instead of 0.2 ml per trigger-movement of the pistol-type syringes; the operator variability and the potential for postinjection complications being thus reduced. Nevertheless, even these PDL-syringes allowed the dentist to force the injection and to create unwanted effects – result of the “lever” system (see Fig. 3).

As a consequence a syringe type without a “lever” was developed: instead a “wheel” aided the operator during his administering of the anesthetic solution and allowed him to adapt the applied force – necessary to overcome the back-pressure of the periodontal tissue – precisely to the individual anatomic situation of the patient.

TOBIEN and SCHULZ (23) (2000) checked in an examination at fresh pig jaws whether the injection pressure can be adapted with this novel syringe to the anatomical structure in such a way that undesired effects can be avoided. The measured values show that the time factor has a considerable

Walton and Abbott in (24) investigated in 1981 that injections with periapical ligaments were superior to those reached with new syringes. Malamed (18) (1982) compared ordinary syringes with, at that time, new syringes – Peripress and Ligmaject. Results, obtained with the use of new syringes, were somewhat higher, especially when comparing the results of conventional syringes of the pistol-type SoftJect and Gabka (14) (1994), the operators used pistol-type syringes.
influence on the injection pressure to be built up for overcoming the tissue resistance in the course of injection of a defined volume. The back-pressure to be overcome reduces with increased injection time (see Table 3).

Evidently, the tissue slowly resorbs the injected volume, so that the back-pressure of the tissue is lowered when the injection time is longer.

A random study was executed by the University of München (MARSHALL (19) 2001) to ascertain the suitability of the SoftJect injection system for clinical use. MARSHALL emphasizes that the reduced injection pressure being applied with the dosing-wheel syringe, represents an advantage with regard to possible damage of the periodontium. The success rate obtained was similar to those of high pressure instruments (pistol-type syringes). The SoftJect has proven its suitability for intraligamentary anesthesia.

Being very familiar with the method of the intraligamentary anesthesia and using it frequently as a standard procedure in his dental practice for years, ZUGAL (27) (2001) compared the – up to that date – state of the technique

<table>
<thead>
<tr>
<th>Dosing-wheel syringe</th>
<th>Intraligamentary anesthesia + ILA</th>
<th>IANB</th>
<th>Infiltration anesthesia</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cases / teeth</td>
<td>202 cases</td>
<td>202 cases / 316 teeth</td>
<td>225 cases / 278 teeth</td>
</tr>
<tr>
<td>Maxilla</td>
<td>73 teeth</td>
<td>-</td>
<td>272 teeth</td>
</tr>
<tr>
<td>Mandible</td>
<td>129 teeth</td>
<td>316 teeth</td>
<td>6 teeth</td>
</tr>
</tbody>
</table>

Questions

<table>
<thead>
<tr>
<th>Anesthesia completed initial, Success rate (%)</th>
<th>187 cases (92.6 %)</th>
<th>160 cases (79.2 %)</th>
<th>196 cases (87.1 %)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average injection quantity?</td>
<td>0.43 ml</td>
<td>1.84 ml</td>
<td>1.67 ml</td>
</tr>
<tr>
<td>„Injection pain?“*</td>
<td>13 cases</td>
<td>42 cases</td>
<td>58 cases</td>
</tr>
<tr>
<td>(6.4 %)</td>
<td>(20.9 %)</td>
<td>(25.8 %)</td>
<td></td>
</tr>
<tr>
<td>„Injection latency time?“*</td>
<td>Practically none</td>
<td>3.95 min.</td>
<td>4.32 min.</td>
</tr>
<tr>
<td>99 %</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>„Duration of anesthesia?”*</td>
<td>&lt; 30 min.</td>
<td>3.86 h</td>
<td>2.98 h</td>
</tr>
<tr>
<td>=Limitation of disposability</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

*1 According to the patients Origin: BW SanAmt, T.Dirnbacher, Jena: Diss.2002

Первоначально оба инъектора - Citoject и SoftJect - применялись примерно одинаково. В ходе клинической практики шприц с дозатором колесного типа SoftJect оказался более чувствительным и более пригодным для достижения анестезии.

За счет прямой передачи давления - без промежуточного использования рычажного механизма - сила обратного давления, которую нужно было преодолеть, ощущалась непрерывно. Причины более или менее выраженно го обратного давления, которое необходимо было преодолеть, являлись анатомические особенности тканей. В случае чрезмерного обратного давления стоматолог мог выбрать другую точку инъекции, где обратное давление и плотность ткани были бы меньше (см. рисунок 4).

Учитывая полученные результаты, в Bundeswehr (Вооруженных
Initially, the customary injection systems Citoject and SoftJect were applied about equally for the injections. In the course of the practical application the dosing-wheel syringe SoftJect proved to be sensitive and more favorable for achieving the intended anesthesia results. On account of the direct pressure transmission – without intermediate successive lever usage – the pack-pressure to be overcome was felt continuously without impediment. The reasons for the reduced, or increased, back-pressure to be overcome were partly due to the different anatomical conditions. In the case of excessive back-pressure the dentist was in a position to select a different injection point, where the back-pressure to be overcome was less and the tissue density lower (see Fig. 4).

Based on these surprising findings the Bundeswehr decided to compare the method of periodontal ligament injection using the dosing-wheel syringe SoftJect, with the conventional anesthesia methods: inferior alveolar nerve block (IANB) and infiltration anesthesia, used as standard local anesthesia method for pain control in dental treatments (3, 4, 26). The aim was to find out whether the unwanted side-effects of the conventional dental local anesthesia methods could be avoided by applying the Soft-ILA (intraligamental anesthesia by using the dosing-wheel syringe SoftJect) - mainly whether the reduced availability of the soldier treated dentally under the conventional local anesthesia methods could be avoided.

In scientific cooperation with the Friedrich-Schiller-University of Jena two evidence based comparison studies have been completed and published (3, 4, 26).

Both studies show a significant difference between the conventional anesthesia methods and the intraligamental anesthesia applied by using dosing-wheel syringes, e. g. of the type SoftJect (see Table 4, 5).
To reduce the limitation of availability of the soldiers after dental treatment under local anesthesia, the authors suggest providing continuing studies to all practicing dentists of the Bundeswehr to become familiar with this anesthesia method, to equip the dental surgeries with this armamentarium and to apply/recommend this anesthesia method as the primary method of local dental anesthesia, except for long duration and large-scale surgical treatments where the ILA cannot fulfill the requirements of pain control.

To compare and to evaluate the various mechanical armamentaria for intraligamental injections (Fig. 3, 4 and 5) CIDES et al. (2009)(2) documented the therapy of 321 cases (teeth) that had been anesthetized by periodontal ligament injections (ILA) prior to teeth conserving treatment.

The success rate including ILA-completion was 99.4 %, one case could be completed by an IANB, in one case no analgesia could be reached not even by IANB (phobia patient). The results show that as well the infiltration as the IANB-anesthesia could be replaced without any restriction by the intraligamentary anesthesia (see Table 6).

Conclusions
Referring to the Status report presented by J. A. GIOVANNITTI and T. A. NiQUE (11) and published in February 1983 regarding the periodontal ligament injection technique, it can be stated – 25 years later – that this technique in fact is an effective means of producing adequate pulpal anesthesia for dental procedures. This method of local anesthesia is objectively superior to the conventional anesthesia methods. However, it has to be emphasized, that the injection technique being necessary for reaching successful intraligamentary anesthesia needs to be learned and trained. Most modern injection instruments – e. g. dosing-wheel syringes – help the operator to be successful. The postoperative unwanted effects such as elongation feeling or pre-contact are due to inadequate instruments which permit the user to inject with too a high pressure; they are iatrogenic.

The dosing-wheel syringes are adapted specifically to the needs of minimal invasive intraligamental injections. They are offering to the operator the advantage to feel in his thumb – similar to a conventional syringe – the back-pressure of the periodontal tissue to be overcome and thus being able

Wыводы
Ссылаясь на тезисы доклада, представленного J.A. Giovannitti и T. A. NiQue (11), (опубликован в феврале 1983 года), и посвященного технике инъекции в периодонтальную связку, можно сказать - 25 лет спустя - что данная техника действительно является эффективным средством обезболивания пульпы зуба при стоматологических процедурах.

Данный метод местной анестезии объективно превосходит обычные методы обезболивания. Однако, следует подчеркнуть, что для эффективного обезболивания путем интраментарной инъекции необходимо в совершенстве владеть ее техникой проведения. Большинство современных инструментов для инъекций, как, например, шприц-дозатор колесного типа способны помочь стоматологу провести эффективную анестезию. Послеоперационные нежелательные эффекты, такие, как, например, чувство онемения, болевой синдром, могут быть вызваны не подходящими инструментами, которые позволяют вводить анестетик с со слишком высоким давлением (внезапные осложнения). Шприцы с дозатором колесного типа специально приоспособлены для потребностей малоинвазивных интралигментарных инъекций. Их преимущество в том, что оператор чувствует своим большим пальцем - по аналогии с обычным шприцем - обратное давление периодонтальных тканей, которое необходимо преодолеть, и, таким образом, адаптировать давление инъекционного раствора к индивидуальным анатомическим особенностям пациента. Эффективность метода обусловлена непрерывностью поступления анестезирующего раствора в периодонт.

Стабильность результатов ИЛА обусловлена готовностью стоматолога изучать и применять на практике указанный метод (аналогично обычным методам анестезии).
Особенности техники ИЛА и использование различных специальных шприцов были хорошо изучены и представлены Glockmann и Taubenheim (12)(2002) и Zugal (27)(2001).

Научное подтверждение возможности широкого применения данного метода осуществляется с 1983 года. Было доказано, что ИЛА имеет ряд преимуществ перед обычными методами местной стоматологической анестезии (проводниковой и инфилтрационной). Все обширные требования к проводимым исследованиям были полностью выполнены.

Ныне ИЛА рекомендована для использования в качестве основного метода обезболивания...
Dental Anesthesia

Table 6: 72.4 % (233 cases) of the intraligamentary anesthetized teeth were situated in the lower jaw, 88.8 % of them (207 cases) would normally have been anesthetized by IANB.

Consistently favourable results are the outcome of the willingness of the dentist to study and train this method, as he did for becoming familiar with the nerve block and the infiltration anesthesia. The details of the technique and the use of the syringe have precisely been defined by GLOCKMANN and TAUBENHEIM (12) (2002) and by ZUGAL (27) (2001).

Corroboration with scientific evidence for wide-spread application of this technique has been realized since 1983. For the first time it has been proven, that the intraligamentary anesthesia (ILA) is to be rated superior to conventional methods of local dental anesthesia (IANB and infiltration anesthesia). All the defined research demands are completely fulfilled.

Finally, it is recommended that the periodontal ligament injection is used as a primary anesthesia method instead of conventional blocks or infiltration anesthesia, to reduce the risk for the patient and to reach better anesthesia results for the operator. Additionally to adult healthy patients this anesthesia method can be applied to children where cheek and lip biting is a concern and for health compromised patients to reduce the cardiovascular risk. Routine use of the periodontal injection technique is recommended as a main standard, provided the operator possesses adequate material and is trained to use it.

The success of the method depends on the continuous diffusion of the anesthetic solution injected into the periodontium.

to adapt the injection pressure he applies precisely to the individual anatomic situation of the patient.

Table 6: В 72.4 % (233 случая) методом ИЛА были обезболены зубы нижней челюсти, в 88.8 % (207 случаев) они могли быть обезболены методом проводниковой анестезии.

вместо проводниковой и инфильтрационной анестезии, с целью уменьшения риска для пациента и для достижения лучших результатов анестезии стоматологом. Кроме того, указанный метод анестезии может применяться у детей (для устранения проблемы кусания щек и губ), и у пациентов с отягощенным анамнезом для уменьшения риска сердечно-сосудистых осложнений.

ИЛА рекомендуется в качестве основного стандарта анестезии в стоматологической практике, при условии, что стоматолог имеет соответствующую квалификацию и оснащение.
Fig. 5: ILA-syringes of the pistol-type with pressure-limitation.
Two outstanding media for your success.

German Medical Journal
Digital Edition Russian/English, the Special Interest Journal about German medicine.
www.german-medical-journal.eu

German Medical Online, the ground-breaking Online Platform for the International Community.
www.german-medical-online.com
Depression

Improving the Care of Depressed Patients and Preventing Suicides - The European Alliance Against Depression

Key problems in treating patients with MD
Under diagnosis and under treatment of depression are well recognized problems, resulting from disease related factors that influence problems in European countries (10) having a major impact on patients (11) and economic resources (12). Because of the described overlap, it is not surprising that improving the care of depressed patients is considered to be an effective approach to prevent suicidality (13). Evidence for this has been provided by the pioneering Gotland-study (14) and more recently by the Nuremberg Alliance against Depression (15,16).

Key problems in treating patients with MD
Under diagnosis and under treatment of depression are well recognized problems, resulting from disease related factors that influence

Keywords:
Depression, Suicidality, community based intervention, European Network, suicide

Depression and Suicide - a challenge for health care systems
Major depression (MD) is a prevalent disorder with, in most cases, a recurrent or chronic course. According to the WHO (1,2) unipolar depression is projected to be ranked as one of the top two leading causes of disability adjusted life years in 2020. Depressive disorders are life threatening due to a high risk of suicidal behaviour and other direct and indirect contributions to mortality (3,4,5) and are responsible for a large part of the annually 54,000 completed suicides in Europe (6,7,8). But this is only the tip of the iceberg. For any suicide, about ten suicide attempts can be registered, which poses a considerable financial burden on the public health system (9).

These facts lead to the conclusion that depression and suicidality are two largely overlapping and important public health problems in European countries (10) having a major impact on patients (11) and economic resources (12). Because of the described overlap, it is not surprising that improving the care of depressed patients is considered to be an effective approach to prevent suicidality (13). Evidence for this has been provided by the pioneering Gotland-study (14) and more recently by the Nuremberg Alliance against Depression (15,16).

The basic principle of this model project, that achieved a reduction of suicidal acts by more than 30 % by implementing a four-level intervention programme, was picked up and further complemented by new intervention materials within the European Alliance Against Depression (EAAD) funded by the European Commission (17,18).

Key problems in treating patients with MD
Under diagnosis and under treatment of depression are well recognized problems, resulting from disease related factors that influence
help seeking behaviour (e.g. hopelessness, lack of energy, feeling of guilt, shame), from lack of knowledge in the general population, in patients (e.g. unjustified concerns regarding psychotherapy or antidepressants), in gatekeepers and in health professionals (19,20,21) as well as structural problems in the health care system (e.g. financial barriers) (22,23). The EAAD 4-level programme simultaneously targets these different aspects.

Basic components of the 4-level approach

Level 1 – Co-operation with GP’s
Interactive workshops with developed educational packages are offered to General Practitioners (GPs). Screening tools are also handed over to GPs together with other materials, i.e. leaflets and brochures. One of three professionally produced videotapes inform GPs about the diagnosis and treatment of depression with the aim to promote early recognition of depression, inform the public about this disorder and to motivate depressed subjects to seek help.

Level 2 – Public Relations
A professional public relations campaign is established including posters at public places, leaflets, infor-ma-tion bro-chores, cinema spots and several public events to inform the public about depression with the aim to promote early recognition of depression, inform the public about this disorder and to motivate depressed subjects to seek help.

Level 3 – Co-operation with Community Facilitators
Educational workshops are provided to important community facilitators such as teachers, counsellors, priests, geriatric nurses, policemen, pharma-cists, and others. Also, a close co-operation with the media is established in order to avoid dangerous reporting inducing imitation suicides (Werther effect). Evidence based guidelines are handed out to local media, providing information how to report appropriately on suicide and attempted suicide.

Level 4 – Cooperation with high risk groups

Fig. 1: 4-level approach
Level 4 – Support for self-help and high risk groups
After a suicide attempt patients receive an “emergency card”, indicating a telephone number which allows an easy and round the clock access to front-line volunteers in life-lines and professional help offered by a specialist. New self-help activities, and support already existing self-help activities, are established.

Implementation strategy
A detailed handbook on how to start and implement the described 4-level-approach has been worked out, comprising three steps (Fig.2): a) Planning and designing a strategy, b) Preparation of the planned interventions like e.g. involvement of patrons, integration of relevant institutions, adaptation of materials and training lectures, planning and locating first public events, contacting the press/media and, c) the implementation phase.

The last starts with an opening event followed by the elements of the 4-level approach like educational trainings of GP’s, workshop for multipliers, lectures, distribution of materials, self-help activities, installation of a hotline for patients after a suicide attempt, etc. Evaluation concepts and materials have been compiled.

Expanding the 4-level approach nationwide
The aim is to expand the 4-level approach from one model region to multiple regions and/or nationwide. This can be done by founding an umbrella organization which supports new regions starting alliances against depression by providing materials, train-the-trainer session, advice and the organization of regular regional and national meetings in order to exchange experiences and to optimize the interventions.

A key element of the success of EAAD is the strong bottom-up element. It is driven by the identification of the regional organizers and initiators with their regional alliance and is an important element in the process of dissemination from regional to multi-regional or national activities against depression and suicidal behaviour.

Evaluation
Evidence concerning the efficacy of the 4-level-approach has already been delivered during the Nuremberg Alliance Against Depression. The 2-years intervention in Nuremberg provided help from volunteers «first line» and professional help from specialists. Such an approach is supported by the new self-help activities, and support already existing self-help activities, created.

Evaluation
Evidence concerning the efficacy of the 4-level-approach has already been delivered during the Nuremberg Alliance Against Depression. The 2-years intervention in Nuremberg provided help from volunteers «first line» and professional help from specialists. Such an approach is supported by the new self-help activities, and support already existing self-help activities, created.

Распространение 4х-уровневого метода по всей стране
Цель заключается в распространении 4-х уровневой программы, внедренной в одном регионе, на несколько регионов и / или по всей стране. Это может быть сделано путем основания головной организации, которая поддержит новые регионы, открывая отделения в регионах и предоставляя им материалы, обучая инструкторов, проводя регулярные региональные и национальные совещания в целях обмена опытом и для координации мероприятий.

Одним из ключевых элементов успеха программы EAAD является структурирование «снизу вверх», то есть выявление региональных организаторов программы, что очень важно для ее распространения на мульти-региональный и национальный уровень.

В каждом регионе альянс организует инициативную группу, которая является важным элементом в процессе распространения программы на региональном и национальном уровнях.

Оценка
Оценка эффективности 4-х уровневой программы уже была проведена Нюрнбергским Альянсом борьбы с депрессией. Мероприятия проводимые в течение 2х лет в Нюрнберге, привели к статистически значимому сокращению...
Depression was associated with a statistically significant and clinically highly relevant reduction in the number of suicidal acts compared to the baseline year 2000 (2002 vs. 2000: -24%, P<0.005) as well as compared to a control region (15). The effect was sustained and even numerically more pronounced in the follow-up year 2003 (2000 vs. 2003: -32.4%) (16).

Achievements
To date the 4-level approach has been implemented in nearly 100 regions in 17 countries in Europe. Additional evaluations within EAAD projects showed that EAAD material can be readily adapted to different cultures (e.g. 18, 24). The strong bottom-up approach helps community members to identify with the local alliance against depression and this boosts motivation and civil commitment as well as self-help.

The European Commission (EC) recommended the EAAD project as best practice example to reduce suicidality in its Green Paper on Mental Health in 2005 (25) and mentioned EAAD in the consensus paper „Prevention of depression and suicide“ (26); moreover EAAD received the European Health Forum Gastein Award in 2007.

Sustainability
To ensure sustainability after the EC-funded project EAAD, the society European Alliance Against Depression with headquarters in Germany, was founded (www.eaad.net). In addition to further implementation of the 4-level approach, further research projects will be conducted, such as the current project OSPI (www.ospi-europe.com). OSPI is a collaborative research project funded by the European Commission under FP7 with the goal to provide EU members with an evidence based prevention concept for suicidality. Further on concrete materials and instruments for running and evaluating these interventions and recommendations for the proper implementation of the intervention will be developed and disseminated.

How to join EAAD?
New partners from Europe or outside Europe, who intend to use the EAAD approach for own intervention activities, are welcome. For further information’s please visit the website www.eaad.net.

projekta, было основан Европейский Альянс по борьбе с депрессией со штаб-квартирой в Германии (www.eaad.net). Кроме того, для дальнейшей реализации 4-х уровневого метода, будут проведены исследования, как, например, реализующийся в настоящий момент проект OSPI (www.ospi-europe.com). OSPI является совместным исследовательским проектом, который финансируется Европейской Комиссией в рамках FP7 с целью предоставить странам-членам ЕС научно обоснованную программу профилактики суицидальности. В дальнейшем будут разработаны и распространены материалы, руководства и рекомендации для надлежащего проведения и оценки этих мероприятий.

Как вступить в EAAD?
В EAAD Приглашаются новые партнеры из Европы или за пределами Европы, которые намерены использовать метод EAAD в своей работе. За дополнительной информацией, пожалуйста, посетите наш веб-сайт www.eaad.net.

Сustainability
To ensure sustainability after the EC-funded project EAAD, the society European Alliance Against Depression with headquarters in Germany, was founded (www.eaad.net). In addition to further implementation of the 4-level approach, further research projects will be conducted, such as the current project OSPI (www.ospi-europe.com). OSPI is a collaborative research project funded by the European Commission under FP7 with the goal to provide EU members with an evidence based prevention concept for suicidality. Further on concrete materials and instruments for running and evaluating these interventions and recommendations for the proper implementation of the intervention will be developed and disseminated.

How to join EAAD?
New partners from Europe or outside Europe, who intend to use the EAAD approach for own intervention activities, are welcome. For further information’s please visit the website www.eaad.net.
Depression

Authors
Prof. Dr. Ulrich Hegerl
Dept. of Psychiatry
University Hospital Leipzig
Germany

Dr. Ella Arensman
National Suicide Research Foundation
Cork, Ireland

Esa Aromaa
Vaasa Hospital District and National Institute for Health and Welfare, Psychiatric Unit of Vaasa Central Hospital, Vaasa, Finland

Prof. Dr. James Coyne
Dept. of Psychiatry, University of Pennsylvania, School of Medicine
United States

Prof. Dr. Ricardo Gusmão
CEDOC, Department of Saúde Mental, Faculdade de Ciências Médicas, Universidade Nova de Lisboa
Lisboa, Portugal

Prof. Dr. Maria Köpp
Semmelweis University (Budapest), Institute of Behavioural Science
Budapest, Hungary

Prof. Dr. Margaret Maxwell
University of Stirling, NMAHP Research Unit, Department of Nursing and Midwifery, Iris Murdoch Centre
United Kingdom

Prof. Dr. Ulrich Meise
Gesellschaft für Psychische Gesundheit
Innsbruck, Austria

Dr. Roger Pycha
Autonome Provinz Bozen-Südtirol – Gesundheitsausserrat
Bozen, Italy

Prof. Dr. Charles Pull
Centre Hospitalier de Luxembourg
Luxembourg

Dr. Thomas Reid
Universitätsklinik und Poliklinik für Psychiatrie
Bern, Switzerland

Dr. Gert Scheerder
Katholieke Universiteit Leuven, LUCAS
Leuven, Belgium

Menike Sisask
Estonian-Swedish Mental Health and Suicideology Institute
Tallinn, Estonia

Dr. Victor Perez Sola
Suicidology Institute
Estonian-Swedish Mental Health and Suicideology Institute
Tallinn, Estonia

Prof. Dr. Chantal van Audenhove
Katholieke Universiteit Leuven, LUCAS
Leuven, Belgium

References

Beautifully located in the sun drenched southwest corner of Germany at the foothills of the Black Forest, Baden-Baden is an elegant, world-famous thermal spa and climatic health resort, wellness and event paradise and cultural metropolis.

Today Baden-Baden is the perfect mix of Belle Époque ambiance and innovative 21st century wellness. Its famous healing thermal water, flowing from 12 springs, is not only used for well-tried therapies but also for modern and innovative treatments. Today the up to 68° degrees hot and healthful water pampers guests from all over the world in the two thermal baths – the modern Caracalla Spa and the historic Roman-Irish “Friedrichsbad.” Furthermore many spa-hotels are particularly conducive to relaxation, offering unique wellness opportunities as well as individual health and wellness treatments.

Eight highly qualified clinics with different focuses and medical specialists with high reputation offer individual medical Check-ups, subject-specific consultation, comprehensive prevention and rehabilitation methods to the point of medical necessary operations. Individual and culture-related wishes of the guests will be considered at any time.

For more than 350 years the three kilometre splendidous parks and gardens “Lichtentaler Allee” has been Baden-Baden’s green and blooming visiting card. The masterpiece made of trees, fountains and flowers invites not only for healthy walks in crystal Black Forest air but also fascinates. Красиво расположенный в солнечном юго-западном «углу» Германии, в предгорьях Шварцвальда, Баден-Баден остается самым элегантным, всемирно известным бальнеоклиматическим курортом, wellness-раем и центром культурной жизни. Сегодня Баден-Баден является идеальным сочетанием атмосферы «бель-эпок» и инновационного оздоровления XXI века. Его знаменитая целебная термальная вода, вытекающая из 12 источников, используется не только для традиционной бальнеотерапии, но и для современных и инновационных методов лечения. Горячая лечебная вода, температура которой достигает 68 оС, балует гостей со всего мира двух термальных купальнях – современной Caracalla Spa (Спа Каракаллы) и исторической римско-ирландской Friedrichsbad (Фридрихсбад). Кроме того, многие SPA-отели, особенно комфортные для проживания и рекреации, предлагают уникальные возможности для оздоровления – общие и индивидуальные процедуры. Восемь специализированных клиник в различных областях медицины, с их высококвалифицированными специалистами отменной репутации, предлагают индивидуальные Check-up’ы (программы диагностики) в сочетании с консультациями, комплексной профилактикой и методами реабилитации, разработанными для каждого пациента. Также в любое время выполняются индивидуальные пожелания гостей, связанные с культурным временпроживанием. На протяжении более 350 лет три километра превосходнейшего парка и сада Lichtentaler Allee (Аллея Лихтенталера) являются зеленой и цветущей визитной карточкой Баден-Бадена.
as a stylish mile for art and culture with the historic “Trinkhalle” (Pump Room), the world-famous “Kurhaus” – the social meeting place of the city – the Casino, the neo-baroque theatre as well as the Museum of Modern Art Frieder Burda designed by star architect Richard Meier. Europe’s second largest opera and concert hall, the “Festspielhaus”, guarantees cultural pleasure at the highest level and offers over 300 top class events yearly.

During the whole year Baden-Baden is setting for outstanding and sophisticated events: Three times a year the International Horse Races, the International Vintage Car Meeting mid of July, outstanding concerts at the parks and gardens “Lichtentaler Allee” and at the romantic courtyard of “Castle Neuweier” as well as international artists and performances at the “Festspielhaus”.

In the picturesque streets and the small lanes of the neo-baroque old town of Baden-Baden, numerous exclusive boutiques invite you to first-class shopping. Everyone who searches for brand products, international labels and individual antiques, jewellery and presents will find himself in the right spot.

Besides well-known starred restaurants, cosy little taverns with local colour and fine Baden cuisine, bistros and countless street cafés in the centre, there is also Baden-Baden’s “Rebland”, one of the most popular Riesling growing districts in Germany and an insider tip for the gourmet and connoisseur of good wines. Germany’s oldest and according to Marlene Dietrich “the most beautiful casino in the world” rounds off a perfect day in a playful manner and entices guests from all over the world to try their luck at the roulette table.

Baden-Baden Kur & Tourismus GmbH
Solmsstrasse 1
76530 Baden-Baden / Germany
Phone: +49 (0) 7221 275 266
Fax: +49 (0) 7221 275 260
bbt@baden-baden.com
www.baden-baden.com

In the picturesque streets and the small lanes of the neo-baroque old town of Baden-Baden, numerous exclusive boutiques invite you to first-class shopping. Everyone who searches for brand products, international labels and individual antiques, jewellery and presents will find himself in the right spot.

Besides well-known starred restaurants, cosy little taverns with local colour and fine Baden cuisine, bistros and countless street cafés in the centre, there is also Baden-Baden’s “Rebland”, one of the most popular Riesling growing districts in Germany and an insider tip for the gourmet and connoisseur of good wines. Germany’s oldest and according to Marlene Dietrich “the most beautiful casino in the world” rounds off a perfect day in a playful manner and entices guests from all over the world to try their luck at the roulette table.

Baden-Baden Kur & Tourismus GmbH
Solmsstrasse 1
76530 Baden-Baden / Germany
Phone: +49 (0) 7221 275 266
Fax: +49 (0) 7221 275 260
bbt@baden-baden.com
www.baden-baden.com

(Festspielhaus) гарантирует зрителям культурное наслаждение на самом высоком уровне и предлагает более 300 событий топ-класса ежегодно. В течение всего года Баден-Баден является местом проведения грандиозных культурных событий: три раза в год проводятся международные скачки, пробег старинных автомобилей в середине июля, великолепные концерты в парках и садах Аллеи Лихтенталера, на территории романтического Castle Neuweier (Замка Нойвейера), выступления зарубежных артистов и исполнителей в «Фестшпильхаусе».

На живописных улицах и в переулках в стиле «neo-бариок» старого города Баден-Баден расположены многочисленные бутики, которые приглашают на переключный шоппинг. Каждый, кто ищет товары известных международных брендов и марок, антиквариат, ювелирные изделия и подарки, оказывается в нужном месте.

Помимо хорошо известных «звездных» ресторанов, на курорте можно найти уютные маленькие таверны с местным колоритом и изысканной кухней, бистро и бесчисленные уличные кафе.

В Баден-Бадене есть и Rebland (Ребланд – одно из самых популярных винодельческих хозяйств Германии, в котором выращивается виноград Рислинг), что является дополнительной «изюминкой» для гурманов и ценителей хороших вин.

Старейшее в Германии и, по определению Марлен Дитрих, "самое красивое казино в мире" может завершить прекрасно проведенный день в форме игры и привлекает со всего мира гостей, желающих испытать свою удачу за столом с рулеткой.
Germany is only seconds away.

Get informed about German clinics, hospitals, medtech, hotels and more.
www.german-medical-online.com
The worldwide presence of German medicine. Germany is only seconds away.

Via QR-Code - the latest cell phone technology - to the direct information on your cell phone. Give it a try.

How it works
Get the reader for your cell phone for free: http://reader.kaywa.com
Take a picture from the QR-Code and jump to the detailed information.

Competence Center for the Diagnostic and Therapy of Chronic Pruritus
Specialists from several Departments of the University offer a complete check-up to identify the origin and best treatment for chronic pruritus.

Department of Obstetrics and Gynecology, University Hospital of Tuebingen
Excellence centre for General Gynecology, Gynecological Oncology, Obstetrics, Urogynecology

Heidelberg University Hospital
One of Europe’s leading medical centers. World-renowned experts provide comprehensive care in all medical specialties.
<table>
<thead>
<tr>
<th>Department / Clinic</th>
<th>Specialty</th>
</tr>
</thead>
<tbody>
<tr>
<td>Department Dermatology and Allergy TUM</td>
<td>Department of Dermatology and Allergy Biederstein, Technical University Munich</td>
</tr>
<tr>
<td>Department of Ophthalmology, Klinikum rechts der Isar, TUM</td>
<td>Diabetic retinopathy, retinal detachment, cataract, corneal transplants, lasik and epilasik and more</td>
</tr>
<tr>
<td>Department of Orthopaedic Sports Medicine, Klinikum rechts der Isar</td>
<td>Knee shoulder and foot surgery, arthroscopy cartilage cell and bone cartilage transplantation</td>
</tr>
<tr>
<td>Department of Pediatric Surgery, University Medical Center Mainz, Germany</td>
<td></td>
</tr>
<tr>
<td>Neurosurgical Clinic, Ludwig-Maximilians-University Munich-Grosshadern</td>
<td>Treatment of multimodal and brain tumours, vascular malformations, paediatric, spine, neurosurgery.</td>
</tr>
<tr>
<td>Pro Vita out-of-Hospital Intensive Care</td>
<td>Intensive Patients Care in a non-hospital setting for adults, babies and children</td>
</tr>
<tr>
<td>Specialist Hospital Kloster Grafschaft</td>
<td>Specialist Hospital for Pneumology and Allergology</td>
</tr>
<tr>
<td>University Hospital for General, Visceral and Transplantation Surgery</td>
<td>Experienced excellence center for abdominal organ transplantation and surgical oncology.</td>
</tr>
</tbody>
</table>
University Hospital Muenster / Universitätsklinikum Münster
The University Hospital of Münster is one of the largest hospital complexes for specialised medical care in northern Germany.

XCell-Center for Stem Cell Therapy
In the Eduardus Hospital

BG-Trauma Hospital Tuebingen
traumatology, endoprosthesis, plastic surgery, cranio-maxillo-facial-surgery, paraplegia, reha

Department Obstet. Gynecology, University Hospital LMU Munich
Women Health, Cancer, Prenatal Care, Infertility

Department of Nephrology and Endocrinology, Charite, Campus Benjamin Franklin
treatment of all kidney problems including renal transplantation and hypertension

Dr. Schlotmann & Partner PraxisKlinik
We are a clinic specializing in Dental Implantology, Dental Aesthetics, procedures under narcosis.

Orthopädie Bavariapark
Center for Arthroscopic Surgery and Minimal Invasive Joint Replacement
<table>
<thead>
<tr>
<th>Company</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>proxomed Medizintechnik GmbH</td>
<td>Professional Training Systems for Active Therapy. Future Rehab and health Concepts</td>
</tr>
<tr>
<td>rB Scientific</td>
<td>...going one step further</td>
</tr>
<tr>
<td>Dieringer GmbH</td>
<td>orthopaedic shoes, orthopaedic inlays for sport shoes, for business shoes, for rheumatism patients</td>
</tr>
<tr>
<td>German Medical Council</td>
<td>German Medical Council organizes the best medical treatment in renowned German hospitals and clinics for you.</td>
</tr>
<tr>
<td>ADAC Service GmbH</td>
<td>When it comes to safety, the ADAC-Ambulance Service is the ideal partner for all holiday and business travellers.</td>
</tr>
<tr>
<td>Reuschel &amp; Co. Privatbankiers</td>
<td>Reuschel &amp; Co. Privatbankiers is one of Germany’s leading private banks</td>
</tr>
</tbody>
</table>
Prof. Dr. Dieter Köhler  
Specialist Hospital Kloster Grafschaft  
Annostrasse 1  
57392 Schmallenberg  
Germany  

Phone: 0049 - 29 72 - 791 - 25 01  
www.krankenhaus-klostergrafschaft.de