Treatment of Gastric Cancer

Лечение рака желудка:
междисциплинарный подход

Treatment of Gastric Cancer - a Multidisciplinary Approach

Клинический случай внутримышечной
ангиомы на руке

Intramuscular Angioma in the Hand – a Case Report

Применение современной
артроскопии для лечения
повреждений плеча

Modern Arthroscopic Treatment Strategies of Shoulder Injuries

Хирургическое лечение холангиокарциномы ворот
печени

Treatment of Hilar Cholangio-carcinoma from the Surgeon’s Perspective
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Contents

Treatment of Gastric Cancer - a Multidisciplinary Approach 12

Intramuscular Angioma in the Hand – a Case Report 22

Drug-eluting Coronary Stents 28

Stent-Grafts in Type B Aortic Dissection 40

Modern Arthroscopic Treatment Strategies of Shoulder Injuries 48

Treatment of Hilar Cholangiocarcinoma from the Surgeon’s Perspective 58

Therapeutic Standards in Colon Cancer 66
Содержание

Лечение рака желудка: междисциплинарный подход

Клинический случай внутримышечной ангиомы на руке

Коронарные стенты с лекарственным покрытием

Применение графт-стентов при B-типе диссекции аорты

Применение современной артроскопии для лечения повреждений плеча

Хирургическое лечение холангиокарциномы ворот печени

Современные стандарты лечения колоректального рака
KLOSTER GRAFSCHAFT

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The hospital Kloster Grafschaft (Grafschaft Abbey) is a special hospital of maximum care for pulmonary and bronchial medicine, respiratory medicine, sleep medicine and allergology. Our extensive technical and personnel equipment on university level allows for this comprehensive diagnostics. In addition, the hospital exhibits two state-of-the-art intensive care units with a total of 14 beds.

**Weaning centre**

One main focus of the hospital is the weaning of long-term respirated patients from the respirator. About 200 patients from intensive care units in whole Germany and partially in European countries are admitted to us usually via helicopter. Our hospital is thus the largest and most successful weaning centre in Germany.

**Pneumology**

In the field of general pneumology, diseases such as bronchial asthma, chronic bronchitis, pulmonary emphysema, pulmonary fibrosis of varying causation, collagenosis with pulmonary involvement, sarcoidosis, bronchial carcinomas, pleural mesothelioma, tuberculosis and pneumonia are diagnosed and treated.

Kloster Grafschaft (Grafschaft Abbey) - клиника, специализированная в области респираторной медицины, лечения заболеваний бронхов и легких, медицины сна и allergологии. Наши современные техническое оснащение и высококвалифицированный медицинский персонал позволяет проводить плановую диагностику и лечение на уровне немецкой университетской медицины. Клиника также располагает двумя блоками интенсивной терапии на 14 мест. Медицинские направления клиники:

**Отключение от искусственной вентиляции легких**

В специализированном центре пациентам с длительной искусственной вентиляцией легких помогают быстро и легко отвыкнуть от аппарата ИВЛ и перейти на самостоятельное дыхание. Ежегодно с помощью вертолета в центр госпитализируются 200 пациентов из блоков интенсивной терапии со всей Германии и стран Европы. Наш центр – самый крупный в Германии по данному виду специализированной помощи.

**Пульмонология**

В клинике проводится диагностика и лечение таких заболеваний, как бронхиальная астма, хронический бронхит, эмфизема легких, фиброз легких различного генеза, коллагеноз с поражением лег
Sleep medicine
The department of sleep medicine specialises in the diagnosis and treatment of sleep-related nightly respiratory disturbances and over-streained respiratory muscular system of varying causation by means of different non-invasive respiratory methods.

Early rehabilitation
A further main focus is the department for early rehabilitation. Long-term respirated patients are rehabilitated here by means of extensive medical treatment, physical therapy, remedial gymnastics and partially speech therapy to an extent that most of them are able to live in their domestic environment again without any help after they have been discharged.

Occupational pulmonary diseases
A department for occupational pulmonary diseases is also integrated in the hospital. This includes the diagnosis and treatment of silicosis, asbestosis and asbestos-related tumour diseases of the lungs and the costal pleura (pleural mesothelioma), chemical-irritant bronchial asthma and chronic bronchitis. This department also contains an extremely efficient medical rehabilitation division.
Allergology
Finally, the hospital has its own allergological department. Allergic asthma, allergic rhinitis, allergic rhinosinusitis, neurodermatitis, eczema, allergic exanthema, urticaria, angioneurotic oedema, contact allergy, intolerance to drugs, drug hypersensitivity, nutritional allergy, insect poison allergy, irritable bowel syndrome and chronic diarrhoea are diagnosed and treated here.

The special hospital Kloster Grafschaft is located in beautiful surroundings in the midst of Schmallenberg in the Sauerland. The rambling, calm and well-kept park of the hospital contributes to your recovery, in addition to the high-quality medical care and treatment.

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Клиника располагает собственным аллергологическим отделением, в котором проводится диагностика и лечение астмы, аллергического ринита, аллергического риносинусита, нейродермита, экземы, аллергической экзантемы, уртикарной сыпи, ангионевротического отека, контактной аллергии, непереносимости лекарств, повышенной чувствительности к лекарствам, пищевой аллергии, аллергии на яд насекомых, синдрома раздраженного кишечника, хронической диареи.

Специализированная клиника Kloster Grafschaft расположена в живописном месте в центре города Шмалленберг района Сауерланда Земли Северная Рейн-Вестфалия. Великолепный парк, окружающий клинику, способствует реабилитации и выздоровлению пациентов.
Treatment of Gastric Cancer - a Multidisciplinary Approach

Лечение рака желудка: междисциплинарный подход
Introduction

The incidence of gastric cancer shows a broad variety worldwide and is the highest in Eastern Asia, Europe and South America. Gastric cancer is less frequent in North America or most parts of Africa [Shi 2010], however, it is still one of the major causes of cancer-related death, and only about thirty percent of patients present in a stage which can be treated with curative intent [Catalano 2009].

Therefore, treatment of gastric cancer requires complete attention by numerous disciplines, all taking together their know-how, with surgeons and oncologists in the center of interdisciplinary activity.

Indeed, surgery and systemic chemotherapy present as mandatory parts of the treatment approach for patients with curatively operable gastric cancer and, in parts, for patients with metastatic disease. This review will give a concise overview on current treatment modalities in case of gastric cancer.

Key words: gastric cancer, treatment, surgery, chemotherapy, survival

Surgery

The primary surgical goal in case of gastric cancer consists of complete (in sano) tumor removal, including appropriate distance of the tumor to the surgical margins. Moreover, the risk for systemic or local cancer recurrence should be diminished by additional lymph node resection. In general, gastric cancer surgery is indicated with curative intent if the tumor has not spread to distant organs i.e. liver, lung, or peritoneum. Endoscopy and CT scan sufficiently provide all required information on tumor histology (including Laurén classification), tumor localisation and resectability. In case of doubt, an explorative laparoscopy may be indicated. Thereby, adequate staging of the patient according to the UICC classification will be achieved.

Early gastric cancer, defined as a lymph-node negative T1 lesion up to 2 cm in diameter with well-moderated differen-

Введение

Заболеваемость раком желудка широко распространена во всем мире и является самой высокой в Восточной Азии, Европе и Южной Америке. Ранее это заболевание встречается в Северной Америке и большей части Африки (Shi, 2010), однако остается одной из основных причин смерти, связанной с раковыми заболеваниями, и лишь около 30% случаев ныне выявляются на стадиях, подходящих к лечению (Catalano, 2009).

Таким образом, лечение рака желудка требует ноу-хау в многочисленных отраслях медицины, в том числе хирургии и онкологии, на базе междисциплинарного медицинского центра. Действительно, хирургия и системная химиотерапия в настоящее время остаются обязательной частью лечения пациентов с операбельным и нерезектабельным раком желудка и у ряда больных с метастатической болезнью. В этой работе дан краткий обзор современных методов лечения рака желудка.

Хирургия

Первичная цель хирургического вмешательства в случае рака желудка – полное (in sano) удаление опухоли с соответствующим расстоянием от нее до хирургического края. Кроме того, риск системного или местного рецидива рака должен быть ограничен путем дополнительной резекции лимфатических узлов. В целом операция при раке желудка показана с лечебной целью, если опухоль не распространялась в отдаленные органы, т. е. в печень, легкие, или брюшину.

Эндоскопия и КТ могут достаточно полно предоставить всю необходимую информацию о гистологической структуре опухоли (в том числе по классификации Ларрен (Lauren)), ее локализации и резектабельности. В случае сомнений показана диагностическая лапароскопия. Только таким путем может быть проведена точная диагностика стадии рака в соответствии с классификацией UICC (Union Internationale Contre le Cancer, Международного союза против рака).

Раннюю стадию рака желудка T1, определяемую как опухоль до 2 см в диаметре, без поражения лимфатических узлов, гистологически умеренно дифференцированную аденоаргину, можно
associated adenocarcinoma, can be successfully treated with curative intent by endoscopic measures such as endoscopic mucosal resection (EMR) or endoscopic submucosal dissection (ESD) [Nakajima 2002]. To identify those patients endosonography is also required for accurate prediction of tumor invasion depth and local lymph node status. Alternatively, proximal gastrectomy with jejunal (pouch) interposition may be performed with survival rates approaching over 90% [Katai 2004, Takagawa 2010].

With respect to locally advanced carcinoma (Figure 1), total gastrectomy as well as subtotal gastrectomy (in case of tumors in the lower third) is recommended, provided adequate tumor distance to the oral and aboral resection margins (according to Laurén classification), confirmed intraoperatively by instantaneous section. Subtotal gastrectomy is comparable to total gastrectomy in terms of postoperative morbidity and mortality. Thus, given equivalent survival, subtotal gastrectomy offers higher quality of life to the patient representing the preferred surgical technique if both are feasible according to intraoperative tumor characteristics. [Shi 2010].

The extent of lymphadenectomy is still discussed controversially since two different approaches were applied. While extended lymphadenectomy was traditionally performed in Eastern Asia, limited lymphadenectomy was advocated by most western surgeons as a result of two large randomized multicenter studies who failed to demonstrate a survival improvement after extended lymphadenectomy, mainly due to increased postoperative morbidity and mortality rates [Bree 2010]. However, a recent multicenter randomized study comparing D1 and D2 lymphadenectomy showed that D2 lymph node dissection was as safe as D1 lymphadenectomy in specialized centers [Degiuli 2010]. Recently published long-term follow up of the randomized Dutch trial comparing D1 versus D2 also favours D2 dissection when splenectomy and pancreactomy are avoided [Songun 2010]. The routine dissection of paraaortic lymph nodes did not prove beneficial in a randomized trial [Sasoko 2008]. Therefore, D2 lymphadenectomy is advised when performed by experienced surgeons, and the addition of paraaortic lymph nodes should be considered only in case of clinical or pathological involvement. Limited (D1) lymphadenectomy however is advocated for surgeons not experienced in extended lymphadenectomy, for patients with poor general performance status, and for early gastric cancer [Bree 2010].

Intestinal reconstruction consists of Roux-en-Y esophagojejunostomy with/out pouch formation. A recent metaanalysis by Gertler et al. reported on clinical advantages of pouch reconstruction after total gastrectomy. Patients with a pouch complained significantly less of dumping and heartburn and showed a significantly better food intake postoperatively. Moreover, quality of life was successfully achieved endoscopically, performing only surgical intervention of the site of interest (Shi 2002).

For resectable (pouch) interposition may be performed with survival rates approaching over 90% [Katai, 2004; Takagawa, 2010].

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Extended surgery for gastric cancer may comprise additional resection of the (transverse) colon, (tail of) pancreas, spleen, or left hepatic lobe [Shchepotin 1998], which can increase postoperative morbidity and mortality rates. Thus, resection of adjacent organs in conjunction with gastrectomy should only be performed to achieve R0 resection, preferably in lymph-node negative patients [Shi 2010]. In carefully selected patients optimal gastric surgery may result in 1-year survival rates of up to 85% when combined with additional systemic chemotherapy [Lin 2008].

Neoadjuvant Treatment
- perioperative chemotherapy

For patients with tumor stage II (UICC) or higher, perioperative chemotherapy is the standard of care. Two large randomized phase III studies demonstrated that a Cisplatin/5-FU based chemotherapy before and after operation improved the 5-year survival rate by 13% or 14% percent, respectively [Cunningham 2006, Boige 2007].

In the MAGIC-trial, 503 patients with adenocarcinoma of the distal oesophagus (14%), the gastro-oesophageal junction (11%) or the gastric body (74%) were randomized between surgery alone and perioperative chemotherapy with Epirubicine/Cisplatin/5-FU. While morbidity and mortality were not increased by additional chemotherapy, the rate of curative resections was increased from 70% (surgery group) to 79%, as was the 5-year survival with 36% (chemotherapy group) compared to 23% (surgery group) [Cunningham 2006]. These results were confirmed in a French study on 224 patients suffering from adenocarcinoma of the distal oesophagus [Shchepotin, 1998]. That less than majority of centers prefer esophageal reconstruction in patients with a pouch, as demonstrated by the Metaanalysis of Gertler et al. [Gertler, 2009]. Treatment with Cisplatin 5-FU significantly improved compared with patients without a pouch [Gertler 2009.] Nevertheless, most centers prefer the Roux-en-Y esophagojejunostomy after (sub-) total gastrectomy.

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In the meantime, different trials are on its way with an attempt to optimize perioperative chemotherapy. Docetaxel has been integrated in the perioperative setting and an interim analysis has showed promising complete remission rates up to 15% [Thuss-Patience 2010]. Other trials have integrated targeted therapy approaches with panitumumab (antibody against the epidermal growth factor receptor EGFR) or bevacizumab (an antibody against vascular endothelial growth factor VEGF), while trials with trastuzumab (inhibition of the HER 2 receptor) in the neo-adjuvant setting will start shortly.

- **Preoperative Radio-Chemotherapy**

For tumors located in the gastric body, there are no phase III trials available addressing the issue of neoadjuvant radiation or chemoradiation, therefore, this concept is no valid option for tumors located in the gastric body.

Several trials included patients with adenocarcinomas arising in the gastro-esophageal junction (GEJ) into preoperative radio-chemotherapy protocols. This approach may lead to a high rate of pathologic complete remissions but is associated with a possible increase in post-operative morbidity and mortality. [Stahl 2009, Gebski 2007, Van Gaast 2010]. In contrast, a perioperative chemotherapy approach does not increase postoperative complication rates and is therefore often the preferred option not only for gastric but also for GE-junction adenocarcinomas.

**Adjuvant Treatment - Postoperative Chemotherapy**

A recent metaanalysis could detect a significant survival benefit for patients treated with adjuvant chemotherapy compared with surgery only [Paoletti 2010]. This benefit could be confirmed in a japanese phase III trial reporting on a survival advantage for patients treated with adjuvant chemotherapy consisting of S1, an oral 5-FU pro drug [Sakuramato 2007]. However, asian patients often show different tumor biology and have different metabolisation of S1 compared to caucasian patients. No single European trial supports the benefit of adjuvant chemotherapy, provided that patients with gastric cancer were well operated including D2 lymphadenectomy and complete (R0) tumor removal [Buzzoni 2006]. A perioperative chemotherapy is therefore the preferred approach in Europe.

**Postoperative Radio-Chemotherapy**

In the USA, postoperative radio-chemotherapy presents as the routine approach based on a randomized phase III study of Macdonald et al. [Macdonald 2001].

**Adjuvant Therapy - Postoperative Chemotherapy**

- **Preoperative Radio- and Chemotherapy**

   Поскольку III фаза клинических испытаний радио- и химиотерапевтических методов лечения опухолей, расположенных в теле желудка, еще не проводилась, указанная концепция лечения пока не является правильным выбором для опухолей с такой локализацией.

   В несколько исследований с предоперационными протоколами радио- и химиотерапии были включены пациенты с adenокарциномой в области желудочно- пищеводного соединения. Такой подход может увеличить показатель полных ремиссий, но связан с возможным увеличением послеоперационной заболеваемости и смертности [Stahl, 2009; Gebski, 2007; Van Gaast, 2010]. Напротив, периоперационная химиотерапия не приводит к увеличению показателя послеоперационных осложнений и, следовательно, зачастую является более предпочтительным вариантом не только для опухоли тела желудка, но и для adenokarcinomas желудочно-пищеводного соединения.

   **Адъювантная терапия - Послеоперационная химиотерапия**

   Недавно проведенный метаанализ позволяет обнаружить значительное увеличение выживаемости у пациентов, получавших адъювантную химиотерапию по сравнению с теми, кому было проведено только хирургическое лечение [Paoletti, 2010]. Это преимущество может быть подтверждено данными III фазы японских клинических испытаний об увеличении выживаемости у пациентов, получавших адъювантную химиотерапию,
However, the results of this trial are not transferable to patients operated under European or Asian standard because of the minimal amount of resected lymph nodes. Indeed, the study of Macdonald et al. had shown that postoperative radio-chemotherapy may be effective with regard to survival improvement compared to surgery alone. However, only 10% of patients in this study had undergone adequate (D2) lymphadenectomy, allowing the interpretation that radio-chemotherapy may be beneficial in worse operated patients at least. Moreover, toxicity was remarkable (41% grade 3, 32% grade 4) [Macdonald, 2001]. So far, no information is available whether adjuvant radio-chemotherapy may also benefit well operated patients, thus, it is currently only recommended in patients suffering from local tumor recurrence or primary R1-tumor resection.

**Palliative Treatment**

*Systemic therapy (1st line chemotherapy)*

In patients with advanced gastric cancer disease palliative efforts are required to prolong survival and to postpone or improve cancer-related symptoms. Four randomized trials were able to show that palliative 1st line chemotherapy improved survival and enlarged life-time with a good quality of life. A meta-analysis of these trials demonstrated that mean prolongation of survival was about 6 months [Wagner 2006]. Currently, combination regiments with cisplatin/fluoropyrimidine with or without epirubicin are regarded as the treatment of choice [Webb 1997, Lutz 2007].

New developments in the last years could bring improvements upon these established chemotherapy regimens. A large randomized phase III study investigated whether intravenous 5-FU could be replaced by oral capecitabine, which is metabolized to 5-FU, and whether cisplatin could be replaced by oxaliplatin. A randomized study on 1,002 patients showed that both changes were possible with equivalent efficacy [Cunningham 2008], later confirmed by other trials [Kang 2009, Al-Batran 2008]. In consequence, the use of oxaliplatin and capecitabine has made chemotherapy more tolerable for patients since toxicity and side effects were reduced.

- **Postoperative therapy**

Inclusion of the S1-peroral ne-activated form of the drug 5-FU (Sakuramato, 2007). Once the use of a gemcitabine-containing adjuvant chemotherapy regimen was shown to be feasible [Cunningham 2006], it became clear that the use of adjuvant chemotherapy regimens with cisplatin/fluoropyrimidine was possible with equivalent efficacy [Macdonald, 2001].

**Table 1: Perioperative Therapy (Phase III Studies)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Regimen</th>
<th>Patient number</th>
<th>5-year overall survival</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>MAGIC</td>
<td>3xFEC→OP→3xFEC vs OP</td>
<td>503</td>
<td>36% vs 23% *</td>
<td>Cunningham 2006</td>
</tr>
<tr>
<td>FNLC</td>
<td>2-3xCF→OP→3-4xCF vs OP</td>
<td>224</td>
<td>38% vs 24% *</td>
<td>Boige 2007</td>
</tr>
<tr>
<td>ECF</td>
<td>Epirubicin, Cisplatin, 5-FU; OP= Operation; CF= Cisplatin, 5-FU; * = significant</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

- **Table 1: Периоперационная терапия (III фаза исследований)**

| Неудовлетворительная эффективность химиотерапии | Статистически значимый

* = significant

**Study Regimen Patient number 5-year overall survival Reference**

| MAGIC | 3xFEC→OP→3xFEC vs OP | 503 | 36% vs 23% * | Cunningham 2006 |
| FNLC  | 2-3xCF→OP→3-4xCF vs OP | 224 | 38% vs 24% * | Boige 2007 |
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**Рак желудка**

- **Паллиативное лечение**

**Системная терапия (химиотерапия 1-й линии)**

У пациентов с запущенным раком желудка паллиативное лечение необходимо для продления жизни, уменьшения симптомов и задержки прогрессирования процесса. В четырех рандомизированных исследованиях удалось показать, что паллиативная химотерапия 1-й линии увеличивает...
A further improvement in terms of chemotherapeutic efficacy was achieved by the addition of docetaxel. Within a randomized phase III study, the triple combination docetaxel/cisplatin/5-FU had significantly improved overall survival compared to the dual combination cisplatin/5-FU [Van Cutsem 2006]. It was also reported that this triple regimen could sustain quality of life better than the dual combination. Nevertheless, the triple combination resulted in an increase of toxicity, especially of diarrhea and neutropenic fever. Therefore, several trials tried to modify this triple regimen to keep the high level of efficacy and to reduce the toxicity profile [Lorenzen 2007, Al-Batran 2008].

- Systemic therapy (2nd line chemotherapy)

Several small phase II trials with different chemotherapeutic agents demonstrated efficacy of 2nd line chemotherapy in gastric cancer. Nevertheless, the attitude towards the benefit of 2nd line treatment for patients is quite different among countries and physicians. The administration of 2nd line chemotherapy varies between 14% in Great Britain, 42% in Europe and USA, and 75% in Asia [Cunningham 2008, Bang 2010, Koizumi 2008].

The benefit of 2nd line chemotherapy regarding a prolongation of survival compared to best supportive care was investigated for the first time in a randomized phase III study of the “Arbeitsgemeinschaft Internistische Onkologie (AIO)”. Although the study did include only 40 patients, a significant survival difference between 2nd line chemotherapy with irinotecan versus best supportive care was demonstrated [Thuss-Patience 2009]. 2nd-line chemotherapy should be offered to patients in a good performance status.

**Targeted Therapy**

Bevacizumab is an antibody against vascular endothelial growth factor. The addition of bevacizumab has resulted in an increase of toxicity, especially of diarrhea and febrile neutropenia. Several small phase II trials showed that bevacizumab could improve quality of life better than the cytotoxic agents demonstrated efficacy [Cunningham, 2008, Bang 2010]. It was also reported that this triple regimen could sustain quality of life better than the dual combination. Nevertheless, the triple combination resulted in an increase of toxicity, especially of diarrhea and neutropenic fever. Therefore, several trials tried to modify this triple regimen to keep the high level of efficacy and to reduce the toxicity profile [Lorenzen, 2007, Al-Batran, 2008].

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**Table 2: 1st- and 2nd-line Palliative Therapy (Phase III Studies)**

<table>
<thead>
<tr>
<th>Study</th>
<th>Patient number</th>
<th>Response Rate (%)</th>
<th>mPFS (months)</th>
<th>mOS (months)</th>
<th>Reference</th>
</tr>
</thead>
<tbody>
<tr>
<td>DCF vs CF</td>
<td>221 vs 224</td>
<td>37 vs 25</td>
<td>5.6 vs 3.7 (mTTP)</td>
<td>9.2 vs 8.6 *</td>
<td>van Cutsem 2006</td>
</tr>
<tr>
<td>XP vs FP</td>
<td>160 vs 156</td>
<td>41 vs 29</td>
<td>5.6 vs 5</td>
<td>10.5 vs 9.3 **</td>
<td>Kang 2009</td>
</tr>
<tr>
<td>FLO vs FLP</td>
<td>112 vs 108</td>
<td>35 vs 25</td>
<td>5.8 vs 3.9</td>
<td>10.7 vs 8.8 ns</td>
<td>Al-Batran 2008</td>
</tr>
<tr>
<td>ECF vs EOX vs ECX vs EOX</td>
<td>263 vs 245 vs 250 vs 244</td>
<td>41 vs 42 vs 42 vs 46 vs 48</td>
<td>6.2 vs 6.5 vs 6.7 vs 7</td>
<td>9.9 vs 9.5 vs 9.9 vs 11.2 **</td>
<td>Cunningham 2008</td>
</tr>
<tr>
<td>CF (CX) vs Trastuzumab vs CF (CX)</td>
<td>290 vs 294</td>
<td>34.5 vs 47.3</td>
<td>5.5 vs 6.7</td>
<td>11.1 vs 13.8 *</td>
<td>Van Cutsem 2009</td>
</tr>
</tbody>
</table>

**2nd-line Palliative Therapy**

| Iritinotecan vs BSC | 21 vs 19 | 0.0 | 2.5 | 4.0 vs 2.4 * | Thuss-Patience 2009 |

The metaanalysis of these studies showed that the maintenance therapy was significantly superior to best supportive care. However, the benefit of 2nd line chemotherapy was not as large as expected. The median overall survival in the best supportive care group was 4.0 months, while it was 2.4 months in the irinotecan group. The median progression-free survival was 2.5 months in the best supportive care group and 4.0 months in the irinotecan group. The median time to progression was 5.5 months in the best supportive care group and 6.7 months in the irinotecan group. The median time to tumor progression was 7 months in the best supportive care group and 9.9 months in the irinotecan group.

**Reference**

Thuss-Patience 2009

**Note:** mPFS = median progression free survival; mTTP = median time to tumor progression; mOS = median overall survival; C = P = Cisplatin; D = Docetaxel; E = Epirubicin; F = 5FU; L = Leucovorin; O = Oxaliplatin; X = Capecitabine; Tras = Trastuzumab; BSC = best supportive care; * = significant; ** = significant for non-inferiority; ns = not significant.
Gastric Cancer

The first targeted therapy with a proven survival advantage in gastric cancer and might be considered in all HER-2 positive patients.

The AVAGAST trial investigating bevacizumab together with cisplatin/5-FU did not result in overall survival prolongation at primary endpoint. Nevertheless, promising efficacy was noted under caucasian patients [Kang 2010]. Accrual of the EXPAND phase III study investigating cetuximab together with cisplatin/5-Fu is nearly completed with over 800 patients randomized, so that results are expected shortly.

The first positive report on a targeted treatment approach in gastric cancer was presented at the 2009 ASCO annual meeting focusing on inhibition of the HER-2 receptor using trastuzumab. In the ToGA-trial 584 patients with HER-2 positive advanced adenocarcinoma of the stomach or gastro-esophageal junction were randomized between a chemotherapy regimen consisting of 5-FU or capecitabine together with cisplatin versus 5-FU/ capecitabine plus cisplatin plus trastuzumab.

Significant prolongation of overall survival from 11.1 to 13.8 months was observed, especially in patients with strong overexpression of HER-2 [Bang 2010]. Thus, trastuzumab is the first targeted therapy with a proven survival advantage in gastric cancer and might be considered in all HER-2 positive patients.

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Intramuscular Angioma in the Hand – a Case Report

Introduction
Dysplasias of the vascular system are frequent congenital malformations. The etiology is unclear. Hemangiomas are benign tumors with an incidence of 12% of all children. A majority of the cases involve females (3♀:1♂) (3). Approximately 15% of hemangiomas have been located on the extremities (9).

Intramuscular angiomas are rare vascular lesions of skeletal muscle, mostly congenitally and constitute less than 1% of all hemangiomas.

At the beginning intramuscular angiomas are frequently asymptomatic until there is a sudden growth spurt in the second or third decade of life (1,20). Mostly the lesion is presented as an enlarging soft tissue mass associated with pain.

Intramuscular angiomas show an expansive growth between the muscle fibres which subsequently destroy the tissue. A malignant infiltrative growth will be simulated. Spontaneous remission is not described and the rate of recurrence is high (16). In conclusion one can say that this is a tumor that does not metastasize instead it grows aggressively, and one therefore assigns intermediary dignity.

Case Report
A 32-year-old woman had a solid and painless swelling in her right hand for 2 years. Over the last few months there was rapid growth. A trauma could not be recalled.

Physical examination revealed a 3x5cm palpable mass in the right thenar which was solid and immovable (Fig.1). There was no redness, discoloration, or inflammation of the skin. The motion in the interphalangeal joint was intact (extension/flexion 0/0/80°), and the metacarpophalangeal joint flexion was reduced (0/0/20°). The opposition of the thumb was possible to the end of the fourth finger. The abduction and adduction were intact, as were perfusion and sensibility.

The X-ray showed a massive compaction of the soft tissue without pressure atrophy of the bone, calcifications or foreign substances in the tumor area.

Введение
Дисплазии сосудистой системы часто являются врожденными пороками развития с неясной этиологией. Гемангиомы – это доброкачественные опухоли, которые встречаются у 12% детей. Большинство случаев выявляются у представительниц женского пола (3♀:1♂) (3). Около 15% гемангиом расположаются на конечностях (9).

Внутримышечные ангиомы – крайне редко встречающиеся поражения сосудов скелетных мышц (в основном врожденные), которые составляют менее 1% всех гемангиом.

Вначале внутримышечные ангиомы бессимптомны, однако в течение второго или третьего десятилетия жизни отмечается их внезапный бурный рост [1,20]. Чаше всего опухоль представляет собой увеличивающуюся мягкую массу, порождающую болевой синдром.

Внутримышечные ангиомы, уничтожая ткани, быстро разрастаются между мышечными волокнами, напоминая инфилтративный рост злокачественных опухолей. Спонтанные ремиссии в литературе не описаны, и частота рецидивов высока [16]. В заключение можно сказать, что эта опухоль не метастазирует, однако растет очень агрессивно, поэтому занимает промежуточное положение между злока- и доброкачественными опухолями.

История болезни
У 32-летней женщины в течение 2 лет на правой руке выявлялась твердая и безболезненная опухоль. За последние несколько месяцев был отмечен ее быстрый рост, что нельзя было связать с травмой. При осмотре в области правой ладони была выявлена четко пальпируемая твердая и неподвижная масса 3 x 5 см (рис.1). Покраснения, обесцвечивания, или воспаления кожи не отмечалось. Движения в межфаланговых суставах были сохранены (разгибание/сгибание 0/0/80°), а в пястно-фаланговых — сокращены (0/0/20°). Оппозиция большого пальца достигала конца четвертого пальца. Отечность и приведение были сохранены, как и кровоснабжение и чувствительность.

Рентгеновское исследование показало массивное уплотнение мягких тканей без атрофии кости, кальцификации и инородных веществ в области опухоли.
The CT scan showed a 45x30mm soft tissue density between the first and second metacarpal bone with a solid structure appearing capsular with signal enhancement after administration of contrast medium. Hypodense inclusions caused an inhomogenous appearance. There were no signs of calcifications or bone participation (Fig. 2).

The operation was under general anaesthesia and the incision occurred via the thenar in a zigzag-form. Intraoperatively we saw a yellow-grey tumor with a soft consistence (Fig. 3). The surrounding musculature was atrophic. The capsule was not sufficient and therefore parts of the M. flexor pollicis brevis, M. abductor pollicis brevis and M. adductor pollicis had to be resected.

Histologic examination showed an intramuscular angioma. In the whole compound, the skeletal muscle was penetrated from newbuilt vessels and mature adipocytes. Characteristic bundles of thick-walled vessels from venous- or arteriovenous type, small venous vessels in a myxoid stroma and tufted capillary proliferations determined the histologic image (Fig. 4).

After a two-week immobilisation in a thumb cast, active and passive physiotherapy was started. Four weeks postoperatively we saw bland scars with intact motion of the thumb (MP-joint 0/0/50°, IP-joint 0/0/80°). Opposition was complete up to the MP-joint of the fifth finger. Abduction and adduction were intact as well (Fig. 5).

Follow-up after one year we saw normal scars in the thenar. Function, sensibility and perfusion were intact. There was no sign of local recurrence.

**Discussion**

Intramuscular angiomas are rare benign vascular tumors. Due to the infiltrative growth and the high rate of recurrence they are classified within the intermediary group according to the new nomenclature.

The first symptoms are most often pain and swelling. In our case there was just a painless tumor and restrictions

KТ-сканирование показало ткань умеренной плотности 45 х 30 мм между первой и второй пястными костьюи с твердой структурой, с капсульным усилением сигнала после введения контрастного вещества. Отмечалась неоднородность ткани за счет эхонегативные включений. Отсутствовали признаки поражения и кальцификации костей (рис. 2).

Операция проводилась под общим наркозом, разрез произведен через ладонь в форме зигзага. Во время операции мы увидели желто-серую опухоль мягкой консистенции (рис. 3). Окружающие мышечные ткани были атрофичными. Капсулы не хватало, поэтому мышцы М. flexor pollicis brevis, М. abductor pollicis brevis и М. adductor pollicis пришлось резецировать.

Обсуждение

Внутримышечные ангиомы – редко встречающиеся доброкачественные сосудистые опухоли. В связи с инфильтративным ростом и высоким показателем рецидива они занимают промежуточное положение в соответствии с новой классификацией. Первыми симптомами чаще всего являются боль и отек. В нашем случае имела место безболезненная опухоль, и ограничения были связаны с отеком, вызвавшем уменьшение объема движений.
were caused by the swelling and subsequent limitation of the range of motion.

Typically for intramuscular angiomas in the MRI and in the histologic examination are the phleboliths. Memis et al reviewed retrospectively the MR imaging studies of 15 patients with intramuscular angiomas. In six of the cases, phleboliths were demonstrated on the plain films or on CT. An evaluation of other characteristics of the tumor like the extent of the lesion or size of the vessels is also possible [14]. Buetow et al show the macroscopic appearance of intramuscular angiomas in the MRI as heterogeneous signals with high and middle intensity [4]. The MRI is the method of choice for diagnostics and planning the operation, but unfortunately in our case a MRI was not available. An outpatient CT scan was only available.

The subdivision of intramuscular angiomas in histologic classifications is based on the size of vessels. We differentiate between the capillary type, the cavernous type and a mixed type. Beham et al [2] showed that the mixed form is most common. In these cases there is a dominating vessel type, as 42% of cases are the venous type. In our case we also had mostly venous vessels. Furthermore, the presence of adipocytes is typical for these tumors. Fat tissue is mainly seen in the cavernous type. A correlation between the localisation of the tumor, the type of vessels and the frequency of recurrence is unknown [2].

In differential diagnosis an angiosarcoma should be considered especially if we have angiomas of the capillary type. Angiosarcomas have no predisposition for age or sex, but can be classified as extremely malignant with a high lethality [16]. Only histological studies can determine the diagnosis. Furthermore one should consider hemangiomas in the differential diagnosis. On physical examination, angiomas of the capillary type are commonly seen as bluish or reddish macules or papules. The size can vary from small lesions to larger plaques. The lesions are usually asymptomatic, but can cause symptoms such as pain or itching.

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cal examination hemangiomas can be wording and have a blue colour under the skin. An infiltrative growth is possible, but destruction usually does not take place.

The diagnostic instrument choice is the sonography, followed by the MRI (5,14,21,22). If the suspicion of a vessel tumor exists, an angiography is recommended, thus providing information about expansion and grade of vascularisation. Only through the angiography is the image of the arterial feeder and the venous drainage possible. Thereby a difference between arteriovenous malformation and other hemangiomas is possible. Caution should however be applied as angiography frequently underestimates the whole expansion of the tumor (17).

One potential therapy is the embolisation of arteriovenous malformations. In the literature however there is only a small number of cases and the rate of recurrence is high. Enjolras et al reviewed retrospectively 200 patients with arteriovenous malformations.

In summary the embolisation alone was not sufficient (7). Herbreteau et al reviewed the results after embolisation of lymphatic malformations. Good results were only noted in 57% of the cases. In 43% a surgical therapy was necessary or recurrence followed (10). Embolisation is a good option in combination with other procedures or prior to a surgical intervention.

Due to the aggressive local growth and the high rate of recurrence we recommend the radical surgical excision of the tumor as the therapy of first choice (6,8,11,13,15,18,19,20). In our case, parts of the thenar muscles are excised for R0 resection. Fast-frozen sections are not always reliable for accurate diagnosis.

If we have small, superficial tumors (≤ 5cm) a primary excision as a radical biopsy is possible. However, if we have larger or deeper tumors a biopsy for definition of the diagnosis is necessary. The tissue sample should be composed of a pseudo-capsule and tumor en-bloc. One disadvantage of have small, superficial tumors (≤ 5cm) a primary excision as a radical biopsy is possible. However, if we have larger or deeper tumors a biopsy for definition of the diagnosis is necessary. The tissue sample should be composed of a pseudo-capsule and tumor en-bloc. One disadvantage of

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the biopsy is the possibility of contamination of the operating area with tumor cells (12), therefore all of the biopsy trajectory needs to be removed in the further operative total excision.

For an optimal hand function, a radical excision performed by a hand-specialist is recommended, so that in the event that functional structures are destroyed an immediate reconstruction is possible. For improvement of opposition, the transposition of the abductor digiti minimi muscle or flexor digitorum superficialis IV muscle is possible. For reconstruction of tendons a transplantation or transposition is an imaginable option. Another good practice is the reconstruction of nerves through suralis transplantation. If necessary, microsurgical procedures for reconstruction are possible in special hospitals.

Conclusion
Intramuscular angiomas are rare tumors with a malignant aspect because of the rapid and infiltrative growth. The following results are functional impairment, pain and deformity. A high rate of recurrence is described. Thus, a radical excision is indicated. Conducting a periodical physical examination is necessary for the exclusion of a recurrence, because serious restrictions of motion, pain or nerve lesions otherwise follow.

Conclusion
Внутримышечные ангиомы являются редко встречающимися опухолями со злокачественным аспектом в связи с их быстрым и инфильтративным ростом. Со временем они вызывают функциональные нарушения, боль и деформации. В литературе описывается высокая вероятность рецидива. Таким образом, при внутримышечной ангиоме показано радикальное удаление.

Fig. 4: histologic examination the skeletal muscle is penetrated from different newbuilt vessels
a: tufted capillary proliferates
b: small, venous vessels with mature adipocytes
c: bundles thick-walled vessels from venous- or arteriovenous type

Fig. 4: Гистологическое исследование: мышцы penetрированы различными сосудами
а – капилляры.
b – мелкие венозные сосуды со зрелыми адипоцитами.
c – лучи толстостенных сосудов венозного или артериовенозного типа.
Fig. 5: postoperative pictures of motion
a: opposition to the MP V joint
b: complete flexion in the IP- and MP-joint of the thumb
c: abduction 60° possible

Literature
Drug-eluting Coronary Stents

Abstract
Drug-eluting stents (DES) have revolutionised the treatment of coronary artery disease by reducing the rate of in-stent restenosis from 20-40% with bare-metal stent (BMS) to 6-8% with DES. However, with widespread use of DES safety concerns have risen due to the observation of late stent thrombosis. With this in mind and better understanding of mechanism and pathophysiology of stent thrombosis, the technological platform, especially innovative anti-restenotic agents, polymeric coatings as well as stent platforms improved with newer DES. Two second-generation DES, Endeavor Zotarolimus-eluting stent (EZS) and Xience-V Everolimus-eluting stent (EES) have provided promising results in both randomized controlled trials (SPIRIT and ENDERAVO) and registries (E-Five, COMPARE) as compared with bare-metal stents (BMS) and first-generation DES. Newer third-generation stent technology, especially biodegradable polymers, polymer-free stents, biodegradable stents on the basis of poly L-lactide (PLLA) or magnesium has been evaluated in preclinical and first clinical trials. However, despite encouraging initial results, long-term data of large-scale randomized trials as well as registries comparing them against currently approved first- and second generation DES are still missing.

Keywords: Drug-eluting stent, everolimus, zotarolimus, stent thrombosis

Introduction
The use of first-generation drug-eluting stents (DES) has substantially reduced angiographic and clinical measures of restenosis both in randomized clinical trial, as well as in large-scale registries over 4 years of follow-up [1-3]. However, with more widespread use of first-generation DES in more complex patients and lesions, serious safety concerns arose [4-9]. Although results of meta-analyses did not reveal significant differences in mortality and myocardial infarction between first-generation DES and bare-metal stents (BMS), the risk of late and very late definite stent thrombosis appeared somewhat increased.

Тезисы
Стенты с лекарственным покрытием (СЛП) произвели революцию в лечении ишемической болезни сердца за счет снижения частоты рестеноза стента с 20–40% при использовании металлических стентов до 6–8% при установке СЛП. Однако в связи с широким использованием СЛП в последнее время, согласно сообщениям, возросла частота поздних тромбозов. С учетом данной информации и новых сведений о механизме и патофизиологии тромбоза стентов была значительно улучшена технологическая основа СЛП, в частности, разработаны инновационные антирестенотические агенты, полимерные покрытия, а также улучшена сама конструкция СЛП. Два СЛП второго поколения: Endeavor Zotarolimus-eluting stent – стент, выделяющий зотаролимус, и Xience-V Everolimus-eluting stent – стент, выделяющий эверолимус, – показали многообещающие результаты в двух рандомизированных контрольных испытаниях (SPIRIT и ENDERAVO) и реестре (E-FIVE) при сравнении с непокрытыми металлическими стентами (НМС) и СЛП первого поколения. Стенты самого последнего, третьего поколения – бесполимерные биостенты из биорассасывающихся полимеров, на основе поли-Л лактида (PLLA) или магния были исследованы в доклинических и первых клинических испытаниях. Однако, несмотря на обнадеживающие первичные результаты, достоверные данные, подтвержденные многолетними крупными рандомизированными исследованиями, а также их сравнение с уже одобренными после испытаний стентами первого и второго поколения до сих пор отсутствуют.

Ключевые слова: стенты с лекарственным покрытием (СЛП), эверолимус, зотаролимус, тромбоз стента

Введение
Использование первого поколения СЛП существенно сократило ангиографические и клинические проявления рестеноза, как в рандомизированных клинических исследованиях, так и в крупных сравнительных 4-летних наблюдениях [1–3]. Однако при более широком применении первого поколения СЛП у пациентов с более сложными случаями визуализацию серьезные опасения относительно их безопасности [4–9].
Early reports from randomized controlled trials, registries as well as meta-analyses using the standardized Academic Research Consortium (ARC) definition, have all indicated that the risk of very late stent thrombosis persists at an annual rate between 0.36% and 0.6%/year to at least 5 years after DES implantation [10-12]. It may be difficult to weight the clinical impact of a rare but serious adverse event of stent thrombosis against a more common, but less acute presentation of in-stent-restenosis. Quantitative comparison with a decision analytic model has identified that, when comparing DES with BMS, a difference as small as 0.14% per year in absolute late stent thrombosis rates over a 4-year period is sufficient to offset any clinical benefit from preventing restenosis [13,14]. Numerous mechanisms might be responsible for acute thrombotic occlusion within the DES-treated segment. Beside individual patient-related factors, lesion characteristics, procedural factors and also device-related factors may impact on the rate of stent thrombosis (Table 1). Conventionally, first-generation DES are coated with permanent polymers that facilitate drug release, but remain on the stent after drug elution. These permanent polymers can cause inflammation with delayed endothelialization, positive remodeling and hypersensitivity reaction, which can culminate in stent thrombosis (Fig. 1). Data from histopathologic studies also indicate that these non-erodable polymers can precipitate stent thrombosis by inducing localized vascular inflammation, hyperesinophilia, thrombogenic reactions, and apoptosis of smooth muscle cells [9,15,16].

As a consequence, in recent years, the focus of clinical research has been on the development of innovative platforms and novel antiproliferative agents requiring a lower dosage of current antimitotic agents, and eventually novel carrier systems including absorbable polymers and/or stents with non-polymeric stent surfaces.

**Second-Generation DESs**

Second-generation DES are typically coated with both new polymers and drugs. Both second-generation DES that are currently approved by the U.S. FDA and EU EMEA, e.g. the Endeavor Zotarolimus-eluting stent (ZEI) (Medtronic Vascular, CA, USA) and the Xience-V Everolimus-eluting stent (EES) (Abbott Vascular, CA, USA), utilize cobalt chro-

Nесмотря на то, что в результате мета-анализа существенных различий по показателям смертности и возникновения инфаркта миокарда при использовании СЛП первого поколения и НМС выявлено не было, риск позднего тромбоза при использовании СЛП все же выше [1, 7–9]. Первые данные рандомизированных контролируемых исследований, а также мета-анализ с использованием критериев Academic Research Consortium (ARC) показали, что показатель риска позднего тромбоза составляет 0,36–0,6% в год в течение 5 лет после имплантации СЛП [10–12]. Возможно, трудно переоценить значение такого редкого, но серьезного осложнения, как тромбоз стента, по сравнению с более часто встречающейся, но менее остры патологией — рестиозом внутри стента. Количественное сравнение СЛП и НМС с помощью аналитической модели продемонстрировало, что даже отлиния показателя позднего тромбоза всего на 0,14% в год в течение 4-летнего периода достаточно, чтобы доказать преимущество применения для предотвращения рестиозы [13, 14]. За возникновение остры тромботической окклюзии в сегменте сосуда с установленным СЛП могут быть ответственны несколько механизмов. Помимо индивидуальных факторов пациента, решающее значение в частоте развития тромбоза имеет специфика повреждения данного сегмента, техническое выполнение процедуры установки стента, а также качество материала, из которого выполнен стент (табл. 1). В состав покрытия СЛП первого поколения входили полимеры, которые облегчали высвобождение лекарственных компонентов, но оставались на стене после растворения медикаментозного слоя. Эти постоянные полимеры могут вызывать воспаление и задержку эндотелизации, ремоделирование сосудов и реакции гиперчувствительности, которые способствуют развитию тромбоза (рис. 1). Данные гистологического исследования подтверждают, что эти нерастворимые полимеры могут ускорить тромбоз, вызывая воспаление сосудистой стенки, гиперэозинофилию, тромбогенные реакции и апоптоз гладкомышечных клеток в месте их локализации [9,15,16].

Вследствие этого в последние годы внимание клинических исследователей было сосредоточено на разработке инновационных платформ и новых антипroliferативных материалов, позволяющих использовать их в меньшей дозировке и с новыми носителями, включая рассасывающиеся полимеры и/или стенты с неполимерными поверхностями.

**Второе поколение СЛП**

Покрытие СЛП второго поколения, как правило, состоит из но-
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non-overlap BMS zone was 1.5±3.4% versus 0.6±2.7% (p=n.s.), whereas these rates were 4.3±11% versus 3.6±8% in the DES zone (n=n.s.). There were no differences in the rates of uncovered/malapposed struts between overlapping BMS and DES, likely the result of fewer uncovered/malapposed struts in ZES patients (0.1±0.4%), which offsets the higher rates observed in SES (6.7%±9.6%) and PES (6.7%±16.5%; p<0.001).

After approving both safety and efficacy in the ENDEAVOR I FIM trial [19] the superiority of ZES compared with BMS was demonstrated in the randomized ENDEAVOR II trial of 1,197 patients with single-coronary artery disease [22]. In comparison with other DES, data have indicated a relatively poor performance of ZES compared with PES and SES at short-term follow-up, as indicated by significantly higher early loss and numerically greater target lesion revascularisation rate (TLR) [23-26]. This might be the result of differences in biological activity of ZES compared with SES. Another potential reason for the observed differences could be more rapid elution kinetics of zotarolimus from the phosphorylcholine polymer; 95% are eluted in approximately 2 weeks, compared with the slower release of sirolimus (95% eluted in approximately 6 weeks) [23-26]. Although in ENDEAVOR IV comparing ZES with PES the overall rate of definite and probable stent thrombosis did not differ during the initial 3 years of follow-up (1.1% vs. 1.7%; p=0.380), there was a significant 1.4% absolute reduction in the rate of ARC definite or probable very late stent thrombosis with ZES compared with PES between 1 and 3 years with continued dual antiplatelet therapy in approximately one-half the patients. Additionally, the rates of cardiac death or myocardial infarction, which were not significantly different at 2 years (3.4% vs. 5.1%; p=0.096), became significant at 3 years (3.6% vs. 7.1%; p=0.004) in favour of ZES [24] (Table 2). The explanation for reduced overall cardiac death and myocardial infarction in ENDEAVOR IV seems multifactorial; patients in the ZES arm revealed significant lower rates of periprocedural myocardial infarction (0.8% vs 2.3%; p=0.014) probably as a result of improved periprocedural sidebranch patency, while the further decrease in myocardial infarction after 1 year (0.7% vs. 2.3%; p=0.017) paralleled the reduction of very late stent thrombosis events. Further

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data will be expected from the randomized PROTECT trial of 8,800 „all-comers” patients assigned to treatment with either ZES or SES [27].

2. The Xience-V EES
The Xience-V EES, receiving EMEA and FDA approval in January 2006 and July 2008, respectively, is based on a CoCr Multi-Link Vision BMS platform (Abbott Vascular, California) coated by a formulation of everolimus, poly-n-butyl methacrylate (PBMa) and a permanent, but biocompatible co-polymer poly-vinylidene fluoride-co-hexafluoropropylene (PVDF-HFP). The drug-polymer coating is applied to the entire stent surface with a standard concentration of 100μg/cm² of stent surface area and is designed to release approximately 80% of the total dose within 30 days of stent placement, with nearly all drug released within 4 months [28].

An experimental study in rabbit iliac arteries revealed more rapid and complete endothelialization with eeS than with SeS, PeS or ZeS. While re-endothelialization of struts at 14 days was variable among comparator stents, significantly greater coverage was seen with EES (66±27.5%), followed by ZES (30.2%±14.2%), PES (26.8%±15.8%), and SES (6.4%±4.2%) (p<0.003 versus EES, and p=0.001 versus BMS) [29].

Clinical data were collected in both real-world registries, and randomized trials comparing eeS to BMS and PES. Results were consistent and demonstrated improved safety and efficacy with EES, together with very low rates of stent thrombosis [30-34].

The SPiRiT ii trial demonstrated better clinical efficacy and safety of eeS compared to the first-generation Taxus express2 PeS over 4 years of follow-up; long-term follow-up demonstrated “delayed” restenosis with EES, a phenomenon previously observed with other DES [35]. This finding, however, did not appear to have any adverse effect on clinical outcomes. In fact, at 3-year

<table>
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<tr>
<th>Patient factors</th>
<th>Acute coronary syndrome</th>
<th>Diabetes mellitus</th>
<th>Renal failure</th>
<th>Impaired left ventricular function</th>
<th>Discontinuation of dual antiplatelet therapy</th>
<th>Clopidogrel Non-responder</th>
<th>Advanced age</th>
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<tr>
<td>Lesion characteristics</td>
<td>Lesion/stent length</td>
<td>Bifurcation lesion</td>
<td>In-stent restenosis</td>
<td>Chronic total occlusion</td>
<td>Bypass-graft intervention</td>
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<td>Procedural factors</td>
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<td>Incomplete stent apposition</td>
<td>High thrombus burden</td>
<td>Multiple stents</td>
<td>Positive remodeling</td>
<td>Residual dissection</td>
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<tr>
<td>Device factors</td>
<td>Hypersensitivity to drug coating or polymer</td>
<td>Incomplete endothelialization</td>
<td>Stent design</td>
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<th>Table 1: Predictors for stent thrombosis</th>
<th>Таблица 1: Предвестники тромбоза стента</th>
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<td>Patient factors</td>
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<td>Device factors</td>
<td>Hypersensitivity to drug coating or polymer</td>
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2. Xience-V-эверолимус выделяющий стент (ЗВС)

Xience-V ЗВС, получивший одобрение EMEA и FDA в январе 2006-го и июле 2008 года соответствственно, основан на платформе CoCr MULTI-LINK VISION BMS (Abbott Vascular, California). Покрытие стента состоит из эверолимуса, поли-N-бутилметакрилата (ПБМА) и постоянного, нерастворимого, но биосовместимого сополимера поли-винилиденфторида-со-гексафторпропилена (PVDF-ГФП). Лекарственно-полимерное покрытие наносится на всю поверхность стента в стандартной концентрации 100 мкг/см² с таким расчетом, что около 80% общей дозы высвобождается в течение первых 30 дней с момента установки стента, а оставшиеся 20% – в течение следующих 4 месяцев [28].

Экспериментальные исследования на подвздошных артериях кролика выявили более быструю и полную эндоцитозацию при установке ЗВС по сравнению с СВС, ПВС или ЗВС. Однако показатели резюмирования в течение 14 дней варировали у сравниваемых стентов, значительно большей показатель был отмечен при ЗВС (66 ± 27.5%), далее по...
follow-up, a greater absolute difference in cardiac death, myocardial infarction, TLR, and major adverse cardiac events (MACE) was observed in favour of EES, when compared with results at both 1- and 2-year follow-up [31]. Similarly, in the larger SPIRIT III trial, the benefit of EES over PES persisted and even increased during follow-up; at 3 years, EES eventually lead to significant reduction in target vessel thrombosis [32] and myocardial infarction, but endpoints of stent thrombosis and TLR did not reduce in secondary TLF versus PES, and significantly lower with eeS than with PES (6.2% vs. 9.1%; HR=0.69; 95% CI 0.50-0.95) driven by a significant reduction of both TVR (6.0% vs. 2.4%; p=0.001) and myocardial infarction (5.4% vs. 2.8%; p=0.007). The rate of definite and probable stent thrombosis was significantly reduced among EES treated patients (0.7% vs. 2.6%; HR=0.26; 95%CI 0.11-0.64; p=0.002). The significant difference in stent thrombosis at 12 months between the two groups was mainly attributable to early stent thrombosis.

3. ZES versus EES
In ESTROFA-2 de la Torre Hernandez et al analyzed 4,768 patients treated with ZES (n=2,549) or EES (n=2,219); the cumulative incidence of definite/probable stent thrombosis for ZES was 1.3% at 1 year and 1.7% at 2 years and for EES 1.4% at 1 year and 1.7% at 2 years (p=0.8), respectively [38]. Increments of definite thrombosis between the first and second year was 0.2% and 0.25%, respectively. Ejection fraction (HR 0.97; 95% CI 0.95-0.99; p=0.008), stent diameter (HR 0.37; 95% CI 0.17-0.81; p=0.01) and bifurcations (HR 2.1; 95% CI 1.14-3.7; p=0.02) emerged as predictors of thrombosis [38]. Serruys et
al compared ZES (n=1,140) and EES (n=1,152) in the Resolute All Comers Trial [39]; ZES was non-inferior to EES with respect to the primary end point which occurred in 8.2% and 8.3% of patients, respectively. The rate of stent thrombosis was 2.3% in the ZES group and 1.5% in the EES (p=0.17) with non-significant differences for in-stent stenosis (21.65±14.42% for ZES vs. 19.76±14.64% for EES) as well as in-stent late lumen loss (0.27±0.43 mm for ZES vs. 0.19±0.40 mm for EES).

Third-Generation Drug-Eluting Stents and Outlook

An extension of above-mentioned concept has been the development of DES that have degradable polymers or are completely free of polymers. Finally, completely biodegradable magnesium and polymeric stents have been developed, which completely disappear once vascular healing has taken place.

One of the newer permanent polymer-coated DESs is the Endeavor Resolute ZES based on a Driver CoCr BMS and coated with a formulation of zotarolimus and a polymer referred to as Biolinx (a blend of 3 different polymers, the hydrophilic C10 polymer to control drug release; the biocompatible and hydrophilic C19 polymer, and polyvinyl pyrrolidone to allow early burst of drug release) [40]. Compared with the permanent co-polymer coating employed by the Endeavor ZES the Biolinx polymer provides improved biocompatibility, increased coating durability and extended drug elution, such that at least 85% of the zotarolimus is released within 60 days, with the remainder being released within 180 days.

Durable polymers used in DES may play a central role in the pathophysiology of impaired healing by triggering a chronic inflammatory reaction; therefore, continuous efforts aim to eliminate permanent polymers. The development of newer biodegradable polymer-coated DES finally resulted in various innovative stents actually being under evaluation. Interest has focused on biodegradable stents because initial after implantation, they theoretically may offer the anti-proliferative benefit of a standard DES, whereas once the polymer has biodegraded within 6-9 months, they may offer the safety of a BMS.

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able poly L-lactide acid (PLLA) polymer. Biolimus is a sirolimus analogue that possesses similar anti-inflammatory properties with exhibiting a higher lipophilic and hydrophobic profile. As such, Biolimus is more rapidly absorbed by the vessel wall. Upon deployment, the drug-polymer formulation is designed to release the drug in a two-phase kinetic with an initial burst release followed by simultaneously sustained drug release and polymer degradation. Both the drug and polymer are fully absorbed within 6-9 months; BioMatrix BES received CE mark approval in April 2008. In May 2007, Terumo Corporation agreed to license the BioMatrix BES, re-branding it as the Nobori BES. After promising results in preliminary studies the BioMatrix Flex BES was further investigated in the randomized multicenter, non-inferiority LEADERS trial [41] encompassing 1,707 patients with chronic stable coronary artery disease or acute coronary syndromes. During follow-up of nine months BES was non-inferior to SES for the primary endpoint (9% vs. 11%; p=0.003 for noninferiority, p=0.39 for superiority). However, frequency of cardiac death (1.6% vs. 2.5%, p=0.22), myocardial infarction (5.7% vs. 4.6%; p=0.30), and TVR (4.4% vs. 5.5%; p=0.29) were similar between both stent types. Moreover, rates for stent thrombosis were similar at all time points and according to any ARC definition. Further promising data in support of a biodegradable polymer were obtained in an OCT substudy, which demonstrated a higher rate of near-occlusive lesions compared to SES [40].

<table>
<thead>
<tr>
<th>Follow-up (months)</th>
<th>Stent</th>
<th>In-Stent-LLL (mm)</th>
<th>Restenosis (%)</th>
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<th>Death (%)</th>
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<th>TLR (%)</th>
<th>Definite/probable stent thrombosis (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>ENDEAVOR I (19)</td>
<td>ZES (n=100)</td>
<td>0.61</td>
<td>5.4</td>
<td>2</td>
<td>0</td>
<td>1.0</td>
<td>2.0</td>
<td>1.0</td>
</tr>
<tr>
<td>ENDEAVOR II (22)</td>
<td>ZES (n=598)</td>
<td>0.61 vs. 1.03*</td>
<td>9.4 vs. 33.5*</td>
<td>7.3 vs. 14.4*</td>
<td>1.2 vs. 0.5</td>
<td>2.7 vs. 3.9</td>
<td>4.6 vs. 11.8*</td>
<td>0.5 vs. 1.2</td>
</tr>
<tr>
<td>ENDEAVOR III (23)</td>
<td>ZES (n=323)</td>
<td>0.60 vs. 0.15*</td>
<td>9.2 vs. 2.1*</td>
<td>7.6 vs. 7.1</td>
<td>0.6 vs. 0.0</td>
<td>0.5 vs. 3.5*</td>
<td>6.0 vs. 3.5</td>
<td>0 vs. 0</td>
</tr>
<tr>
<td>ENDEAVOR IV (24)</td>
<td>ZES (n=773)</td>
<td>0.67 vs. 0.42*</td>
<td>13.3 vs. 6.7</td>
<td>n.a.</td>
<td>1.1 vs. 1.1</td>
<td>1.6 vs. 2.7</td>
<td>4.5 vs. 3.2*</td>
<td>0.9 vs. 0.1</td>
</tr>
<tr>
<td>SORT-OUT III (25)</td>
<td>ZES (n=1,162)</td>
<td>n.a.</td>
<td>n.a.</td>
<td>n.a.</td>
<td>4.4 vs. 3.0*</td>
<td>2.0 vs. 1.0*</td>
<td>6.0 vs. 2.0*</td>
<td>1.1 vs. 0.5*</td>
</tr>
<tr>
<td>E-Five (26)</td>
<td>ZES (n=2,116)</td>
<td>n.a.</td>
<td>n.a.</td>
<td>7.5</td>
<td>1.7</td>
<td>1.2</td>
<td>4.5</td>
<td>0.6</td>
</tr>
</tbody>
</table>

LLL: late-lumen loss; MACE: major adverse cardiac events; TLR: target lesion revascularization
* for significant p-values

Table 2: Overview of trials comparing zotarolimus-eluting stent

Одним из новых представителей СЛП с постоянным полимерным покрытием является Endeavor Resolute ZES, разработанный на основе Driver CoCr НМС с покрытием, содержащим зотаролимус и полимер Biolinx (смесь из 3 разных полимеров: гидрофобного полимера C10 для контроля высвобождения лекарства, биосовместимых и гидрофильных полимеров C19, и поливинилового пиролидона для обеспечения раннего «всплеска элюции» лекарства) [40]. По сравнению с постоянным полимерным покрытием, применяемым для Endeavor ZES, Biolinx обладает более высокой биосовместимостью, долговечностью и характером элюции лекарственного вещества: до 85% зотаролимуса высвобождается в течение 60, а остальная часть — на протяжении следующих 180 дней. Прочные полимеры, используемые в СЛП могут играть центральную роль в патофизиологии нарушения процесса заживления, вызывая хронические воспалительные реакции, поэтому непрерывные усилия исследователей направлены на развитие технологий, позволяющих обойтись без постоянных полимеров. Новые биорассасывающиеся полимерные покрытия в новых поколениях инновационных стентов проходят серьезную оценку и испытания. Интерес сосредоточился на разработках биорассасывающихся стентов, ввиду сочетания в них антипролиферативного действия стандартного покрытия СЛП с безопасностью НМС, так как в течение последующих 6–9 месяцев полимер рассасывается. Коронарный стент BioMatrix BES из нержавеющей стали 316L с биорассасывающимся лекарственным покрытием, состоящим из смеси биолимуса...
Table 3: Overview of trials comparing the everolimus-eluting stent

<table>
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<tr>
<th>Follow-up (months)</th>
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</thead>
<tbody>
<tr>
<td>SPIRIT I (30)</td>
<td>60</td>
<td>EES (n=27) BMS (n=29)</td>
<td>n.a.</td>
<td>16.7 vs. 28.0</td>
<td>0 vs. 7.4</td>
<td>8.3 vs. 0</td>
<td>8.3 vs. 28.0*</td>
<td>0 vs. 0</td>
</tr>
<tr>
<td>SPIRIT II (31)</td>
<td>6</td>
<td>EES (n=223) PES (n=77)</td>
<td>0.11 vs. 0.36*</td>
<td>1.3 vs. 3.5</td>
<td>2.7 vs. 6.5</td>
<td>0 vs. 1.3</td>
<td>0.9 vs. 3.9</td>
<td>2.7 vs. 6.5</td>
</tr>
<tr>
<td>SPIRIT III (32)</td>
<td>12</td>
<td>EES (n=669) PES (n=333)</td>
<td>0.16 vs. 0.3*</td>
<td>92.3 vs. 5.7</td>
<td>6.0 vs. 10.3*</td>
<td>1.2 vs. 1.2</td>
<td>2.8 vs. 4.1</td>
<td>3.4 vs. 5.6</td>
</tr>
<tr>
<td>SPIRIT IV (36)</td>
<td>12</td>
<td>ZEES (n=2,458) PES (n=1,229)</td>
<td>n.a.</td>
<td>4.2 vs. 6.9*</td>
<td>1.0 vs. 1.3</td>
<td>1.9 vs. 3.1*</td>
<td>2.5 vs. 4.6*</td>
<td>0.3 vs. 1.1*</td>
</tr>
<tr>
<td>COMPARE (33)</td>
<td>12</td>
<td>EES (n=897) PES (n=903)</td>
<td>n.a.</td>
<td>6.2 vs. 9.1*</td>
<td>2.0 vs. 1.6</td>
<td>2.8 vs. 5.3*</td>
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Parallel to developing DES with biodegradable polymers, DES completely polymer-free are emerging. Despite the absence of a polymer, these stents are still able to elute antiproliferative drugs in a controlled manner. This is achieved by either dissolving the antiproliferative agent into a nonpolymeric biodegradable carrier on stent surface, impregnating the antiproliferative agent in pure form onto the porous surface of the stent or attaching the antiproliferative agent directly to the vascular tissue surface using either covalent bonding or crystallization/chemical precipitation. Current clinical studies of polymer-free stents are limited; at present only the YUKON DES (Translumina, Hechingen, Germany) is available in Europe, whereas several others are undergoing FIM clinical studies. Clinical data indicate non-inferiority of the YUKON stent when compared with PES at 9- to 12-month follow-up [43,44].

Fully biodegradable stents (BDS) offer several potential advantages over conventional BMS or DES. These include potential reductions in adverse events such as stent thrombosis, because drug elution and vessel scaffolding are only provided by the stent until the vessel has healed, and as such, no triggers for stent thrombosis, such non-endothelialized stent struts, or drug polymers are present long term. The current BDS are composed of either a polymer or a metal alloy.
The most frequently used polymer in the current generation of BDS is PLLA and poly-D,L-lactide (PDLLA), both utilized as resorbable sutures, soft-tissue implants, or orthopedic implant. The PLLA and PDLLA are metabolized via the Krebs cycle over a period of approximately 12 to 18 months and converted to carbon-dioxide and water. At present, no BDS has either the C.E. mark or U.S. FDA approval.

The BVS (Bioabsorbable Vascular Scaffolding) EES (Abbott Vascular) is a manufactured from PLLA polymer and is coated with a formulation of everolimus in a PDLLA polymer matrix which contains and controls the release of everolimus from the stent. The drug-polymer coating is applied to the entire stent surface with a standard concentration of approximately 8.2μg/mm stent length and is designed to release approximately 80% of the total dose within 30 days of stent placement; polymeric strut absorption will take approximately two years. Following encouraging pre-clinical studies, both safety and feasibility of the first-generation BVS implant were assessed in 30 low-risk patients with de novo coronary lesions who were enrolled in the prospective, open-label, multicenter FIM ABSORB study [45]. The study demonstrated clinical safety of the BVS as there was only 1 ischemia-driven MACE at 6 months, whereas no MACE events were reported in the following 30 months. Of note, no stent thrombosis has been observed over 3 years follow-up [46]. At two-year follow-up angiography, the instantaneous loss of 0.48mm and the diameter stenosis of 27% did not significantly differ from the findings at six months. In addition, there is evidence of restoration of vasomotor function in the stented segment [45].

Beside bioabsorbable polymer-coated DES there are bioabsorbable polymer-free stents. The balloon-expandable AMS-1 BDS is composed of 93% magnesium and 7% rare earth metals. The stent has a high mechanical strenght, and has properties comparable to stainless steel stents, such as low elastic recoil (<8%), a high collapse pressure (0.8 bar), and minimal shortening after inflation (<5%) [47]. The PROGRESS AMS study is a multicenter, nonrandomized, prospective study assessing the efficacy and safety of the AMS-1 stent in 63 patients with single de-novo lesions. At 12 months follow-up, there was no death, myocardial infarction, or stent thrombosis, thus confirming excellent safety; in addition, there was also return of vessel vasoreactivity. The rate of MACE was 23.8% and 26.7% at 4 and 12 months follow-up, respectively. Thus, the study achieved its primary end point, but TLR was disappointing at 39.7% at 4-month, and 45.0% at 12-month follow-up [47]. Importantly, the results from this pilot study have been utilized to improve both the design and composition of the stent. Modifications have centered on prolonging stent degradation time and enabling drug elution, thereby reducing restenosis from either negative 4,6, p = 0.30, and TVR (4.4% against 5.5, p = 0.29) were expected by both stents. Moreover, the show that the AMS-1 BDS is more bioabsorbable polymer-free stents. The balloon-expandable AMS-1 BDS is composed of 93% magnesium and 7% rare earth metals. The stent has a high mechanical strength, and has properties comparable to stainless steel stents, such as low elastic recoil (<8%), a high collapse pressure (0.8 bar), and minimal shortening after inflation (<5%) [47]. The PROGRESS AMS study is a multicenter, nonrandomized, prospective study assessing the efficacy and safety of the AMS-1 stent in 63 patients with single de-novo lesions. 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remodelling or from excessive healing response. The new-generation stents consist of the AMS-2 and -3. The AMS-3 stent (DREAMS=Drug Eluting AMS), currently under evaluation, is a modification of the AMS-2 stent, and is designed to reduce neointimal hyperplasia by incorporating a biodegradable matrix for controlled release of antiproliferative drug.

**Conclusion**

On retrospect, safety concerns regarding first-generation DES led to the development of numerous new DES. Interest has focused on second-generation DES because they may theoretically offer the anti-proliferative benefits of a standard DES married to a biodegradable polymer without inflammatory reaction or adverse effects. However, despite promising initial results of both second-generation DES there will be continuously growing technology of newer DES to improve even the performance and safety of currently tested DES. Because the incidence of hard end points does not markedly differ among currently tested DES, one should expect that large controlled studies, real-world registries and/or meta analysis will be required to prove superiority.

80% от общей дозы элюирования в течение 30 дней после установки стента, расстроение же полимерной основы в среднем занимает около двух лет. Обнаруживающие результаты доклинических исследований, подтверждающих возможности и безопасность первого поколения BVS, были получены у пациентов с низким уровнем риска, с первично диагностированным поражением коронарных сосудов в ходе открытого, многоцентрового исследования FIM ABSORB [45]. Исследование показало клиническую безопасность BVS, поскольку был элюирован только 1 случай контролируемой ишемии за 6 месяцев наблюдения, а несерьезные осложнения не были зарегистрированы в следующие 30 месяцев. Следует отметить, что ни одного случая тромбоза стента не наблюдалось уже в течение 3 лет наблюдения [46]. К концу 2 года мониторинга ангиографических данных была обнаружена потеря 0,48 мм стента с диаметром стеноза 27%, что существенно не отличалось от результатов диагностики через шесть месяцев после установки стента. Кроме того, имеются свидетельства восстановления вазомоторной функции стентированного сегмента [45].

Кроме СЛП с биорассасывающимим полимерным покрытием, существуют также биорассасывающие стенты, в составе покрытия которых полимер отсутствует вовсе. Так, покрытие AMS-1 BDS состоит из 93% магния и 7% редкоземельных металлов. Стент обладает высокой механической прочностью и имеет свойства, сравнимые со стентами из нержавеющей стали, такие как низкий уровень эластической тяги (<8%), высокое давление сжатия (0,8 бар), и минимальное укорочение после раздувания (<5%) [47]. PROGRESS AMS проводилось как многоцентровое нерандомизированное проспективное исследование по оценке эффективности и безопасности AMS-1 стента у 63 больных с впервые диагностированным поражением сосудов. За 12 месяцев наблюдения не было зафиксировано ни одного случая смерти, инфаркта миокарда или тромбоза стента, что еще раз подтвердило высокий уровень безопасной. Кроме того, на протезированный участок была восстановлена вазореактивность. Показатели сердечно-сосудистых осложнений составили 23,8 и 26,7% за 4 и 12 месяцев наблюдения соответственно. Однако на момент завершения первого этапа испытания показатель реваскуляризации поражения мишени принес разочарование: 39,7% в течение 4 месяцев и 45,0% за 12 месяцев наблюдения [47].

Важно отметить, что результаты этого пилотного исследования были использованы для улучшения, как дизайна, так и состава стента. Изменения были сосредоточены на продлении времени рассасывания стента и способности препарата, тем самым снижая риск рестеноза или чрезмерной реакции и побочных эффектов. Однако, несмотря на многообещающие первые результаты использования обоих модификаций СЛП второго поколения, не прекращаются разработки еще более совершенного стента, способного превзойти успех СЛП по показателям эффективности и безопасности. Поскольку в серии описанных выше испытаний не было выявлено существенных различий в показателях различных модификаций СЛП, следует ожидать более масштабных исследований и мета-анализа, в которых им предстоит доказать свое превосходство.

Заключение

В ретроспективе проблемы безопасности в отношении первого поколения СЛП привели к созданию множества новых стентов. Интерес сосредоточился на втором поколении СЛП, поскольку теоретически в них сочетаются антипroliferативные свойства стандартного СЛП с преимуществами биорассасывающихся полимеров: отсутствие воспалительной реакции и побочных эффектов. Однако, несмотря на многообещающие первые результаты использования обоих модификаций СЛП второго поколения, не прекращаются разработки еще более совершенного стента, способного превзойти успех СЛП по показателям эффективности и безопасности. Поскольку в серии описанных выше испытаний не было выявлено существенных различий в показателях различных модификаций СЛП, следует ожидать более масштабных исследований и мета-анализа, в которых им предстоит доказать свое превосходство.


**Stent-Grafts in Type B Aortic Dissection**

**Introduction**

Aortic dissection is an uncommon, but highly lethal condition with an estimated incidence of 20 cases per million annually [1-3]. Around 0.5% of all patients with chest or back pain suffer from aortic dissection or its precursors [4]. Men are twice as often found to suffer from acute aortic dissection than women with 60% of dissection cases classified as proximal (type A) and 40% as distal (type B according to the Stanford classification) [1]. Dissection of the ascending aorta is associated with a mortality rate of 1-2%/h within the first 24 hours resulting in a mortality rate of up to 50-74% within the first two weeks [1]. An uncomplicated acute type B dissection is less frequently lethal with survival rates in medically treated patients of 89% at 1 month, 84% within 1 year, and up to 80% within 5 years [1,5]. However, patients with acute or late complications including either malperfusion syndrome with renal failure, visceral or leg ischemia, or contained rupture require urgent repair considering a mortality raising to 20% at day 2 and to 25-50% within 1 month [1].

Similar to type A dissection, advanced age, rupture, shock and malperfusion are important independent predictors of early mortality in type B dissection [6]. While almost every patient with a type A dissection should be managed by open surgery, endovascular concepts have emerged as an alternative to manage aortic dissections, mainly distal thoracic aortic dissection. Conversely, for proximal dissection endovascular approaches (thoracic endovascular aortic repair [TEVAR]) remain anecdotal for localised pathologies in patients unfit for open repair.

This manuscript summarizes results and recommendations for endovascular management of patients with type B aortic dissection.

**Keywords:** aortic dissection, stent-graft, malperfusion, DeBakey, Stanford

**Indications for TEVAR in Type B Aortic Dissection**

The natural course of aortic dissection is determined by two elements, early complications and chronic events. Early complications include rupture, malperfusion, and visceral ischemia, all of which are associated with a mortality rate of 25-50% within the first 2 weeks [1]. These complications are often due to rapid growth of the false lumen, which can lead to visceral ischemia, renal failure, or rupture. The primary goal of endovascular treatment in type B dissection is to prevent these early complications.

**Indications for TEVAR**

1. **Rupture:** Rupture of the false lumen is an absolute indication for TEVAR. This can occur spontaneously or following a traumatic event.
2. **Malperfusion:** Malperfusion syndromes, such as visceral ischemia or renal failure, are significant indications for TEVAR. These conditions can be acute or chronic and result from compression of the true lumen by the false lumen.
3. **Saccular aneurysm:** A saccular aneurysm measuring 4 cm or more in the ascending or descending aorta is an indication for TEVAR. This is to prevent the risk of aneurysmal rupture.
4. **Saddle aneurysm:** A saddle aneurysm involving the ascending aorta is a relative indication for TEVAR, especially if it is calcified or involves the aortic valve.

**Contraindications for TEVAR**

- **Severe co-morbidities:** Patients with severe co-morbidities, such as unstable coronary artery disease, may not be suitable candidates for TEVAR.
- **Inadequate access:** Access to the aorta may be inadequate for stent-graft deployment.
- **Suboptimal anatomy:** Patients with suboptimal anatomy, such as tortuosity or severe aortic valve disease, may not be suitable candidates for TEVAR.

**Conclusion**

Endovascular repair of type B aortic dissection is a viable treatment option for patients with thoracic aortic aneurysms and complications such as malperfusion, visceral ischemia, or rupture. A multidisciplinary approach is necessary to determine the most appropriate treatment strategy for each patient. Further research is needed to improve the outcomes of TEVAR in the management of type B aortic dissection.
Spin-offs comprise any kind of malperfusion syndrome, persistent pains or aortic rupture, while late events are proximal progress or documented false lumen expansion with the risk for late rupture. Once a patient survives the first two weeks after impact of dissection, the dissection is by definition chronic. Acute and chronic dissections may both require similar medical treatment with primarily blood pressure control but even acute dissections can be complicated or uncomplicated.

The feasibility and relatively safety of TEVAR in descending thoracic aorta has already been established as an alternative to surgical treatment of type B aortic dissection [2,3], but due to the lack of both, randomized controlled trials and long-term follow-up data the indications for endovascular strategies remain to be fully defined for dissection (Table 1).

There is clear observational evidence [2,3], that depressurization and shrinkage of the false lumen is beneficial in acute dissection, ideally followed by complete thrombosis of the false lumen and remodelling of the entire dissected aorta (Fig. 1). Similar to historically accepted indications for surgical intervention, scenarios such as malperfusion syndrome, intractable pain rapidly expanding false lumen to a total diameter over 55 mm or signs of imminent rupture are accepted indications for TEVAR in type B dissection [7]. Even in some cases of retrogradely extended distal dissections, stent-graft treatment of the descending thoracic aorta can also be performed as a single primary step or as a staged secondary step after initial surgical repair of the proximal part of the aorta or the arch [2,3]; the surgical part may include an elephant trunk or transposition of arch vessels to allow extended landing zone for endovascular completion of such hybrid approach. In case of a localized retrograde type A dissection originating from an entry tear in the descending thoracic aorta this entry can sometimes be sealed by a transfemoral stent-graft with subsequent remodelling of the entire dissected aorta.

| Surgery | Type A aortic dissection
| - Acute type B dissection complicated by
  - Retrograde extension into the ascending aorta
  - Dissection in fibrilinopathies
    (e.g. Marfan-syndrom, Ehlers-Danlos-Syndrom) |
| Medical | Uncomplicated acute type B dissection
| - Stable isolated aortic arch dissection |
| Interventional | Unstable acute type B dissection
| - Malperfusion
  | - Rapid expansion (>1cm/year)
  | - Critical diameter (>5.5cm)
  | - Refractory pain
  | Aortic dissection due to blunt chest trauma
  | Hybrid procedure for extended type A aortic dissection |

Table 1: Distribution of differential therapeutic strategies in aortic dissection [2,3].

Table 1: Представление различных терапевтических стратегий в лечении диссекции аорты [2,3].

Показания для TEVAR у пациентов с диссекцией аорты

Характер течения диссекции аорты определяется, главным образом, развитием осложнений, ранних и поздних. Ранние осложнения включают все варианты синдрома мальперфузии, перистирующую боль или разрыв аорты, в то время как поздние представлены прогрессирующим расширением ложного просвета с риском его отсроченного разрыва.

В случае, если пациент выживает в течение первой недели после начала диссекции аорты, она классифицируется как хроническая. Как острая, так и хроническая диссекция аорты требуют похожего подхода в ведении пациентов, включая в первую очередь, контроль артериального давления. Острая диссекция может протекать с осложнениями или без.

Обоснованная и относительно безопасная методика TEVAR на нисходящей грудной аорте была разработана в качестве альтернативы открытому хирургическому лечению диссекции аорты В типа [2, 3], но, учитывая недостатки обоих методов, выбор того или иного из них должен основываться на точной диагностике, с учетом соответствующих показаний (табл. 1). Существуют четкие данные [2,3], свидетельствующие о том, что при острой диссекции показана декомпрессия и сужение ложного просвета, с последующим полным тромбозом ложного просвета и реконструкцией всей расслоенной аорты (рис. 1).

В соответствии со сложившимися стандартами, показаниями к применению хирургического вмешательства TEVAR при В типе диссекции аорты, являющихся: синдром мальперфузии, некупируемая боль, быстро расширяющийся ложный просвет диаметром более 55 мм, признаки надвигающегося разрыва [7].

Даже в случае ретроградно расширяющейся диссекции графт-SENTIERING нисходящей части аорты может быть применено в качестве изолированного метода или как второй промежуточный этап первичного хирургического восстановления проксимальной части аорты или дуги аорты [2, 3]; открытая хирургическая часть может включать метод «слона-вьего хобота» или транспозицию
With TEVAR, paraplegia was documented in 0.8%, but is obviously associated with extensive coverage of the aorta beyond 20 cm and with the use of multiple stent-grafts, or in case of previously replaced infrarenal aortic aneurysm [2,3].

**Complicated Acute Type B Aortic Dissection**

While patients with stable acute type B dissection should be managed medically, about 30%-42% of acute type B aortic dissection are complicated as evidenced by hemodynamic instability or peripheral vascular ischemia [8]. Among other complications, acute lower limb and visceral ischemia have been reported in 30%-50%; malperfusion syndrome occurs frequently in cases of distally extended dissections and may lead to death in 50%-85% if left untreated [5,9, 59]. During necropsy of 18 patients with type B dissection full compression of the true lumen with aortic obstruction was evident in 56% [10]. Once diagnosed these complications require emergent therapeutic action; despite a wide array of open surgical strategies, surgical mortality for patients with acute aortic dissection complicated by renal ischemia has been reported in 50%, and in the case of impaired mesenteric perfusion even 88% [2,3,11]. Different treatment strategies, however, may impact on survival; in 571 patients with acute type B aortic dissection 390 (68.3%) were treated medically; among complicated cases 59 (10.3%) underwent standard open surgery, and 66 (11.6%) were treated with an endovascular approach [12]. In complicated cases in-hospital mortality was significantly lower with TEVAR (10.6%) than after open surgery (33.9%; p=0.002), approaching the survival rate of medically treated uncomplicated type B dissection (Fig. 2). Thus, stent-graft repair is an attractive alternative to surgical repair for correcting ischemic complications (Fig. 3). Usually, TEVAR mediated sealing of the entry site in the descending thoracic aorta results in thrombosis of the false lumen and redirection of flow to the true lumen, normalizing distal vessel perfusion and restoring branch vessel patency [13] (Fig. 1). With TEVAR, paraplegia was documented in 0.8%, but is obviously associated with extensive coverage of the aorta beyond 20 cm and with the use of multiple stent-grafts, or in case of previously replaced infrarenal aortic aneurysm [2,3].

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Aortic Dissection

4). The PETTICOAT (Provisional Extension to Induce Complete Attachment) concept takes the idea even further by extending the stent-graft scaffold distally with open-cell bare metal stents. For instance, if malperfusion persists after coverage of the primary entry tear, additional distal open stents were deployed until distal malperfusion is corrected [14].

With this concept aortic fenestration maneuvers or branch vessel revascularization with uncovered stent are usually not needed and obsolete.

The EUROSTAR/United Kingdom registry represents a large series of patients subjected to TEVAR, including 131 patients with aortic dissection (5% proximal, 81% distal and 14% not classified) of which 57% presented symptoms of rupture, aortic expansion, or side branch occlusion, all considered complicated dissection. Although meaningful long-term data are still lacking, technical success was achieved in 89%, at the expense of a 30-day mortality of 8.4% [15]. A series of patients at the Arizona Heart Institute, comprising 40 patients (23 acute and 17 chronic) treated with TEVAR for complicated distal aortic dissection, enjoyed a technical success in 95%. There was one perioperative death due to iliac rupture and one case of paraplegia, while 15 patients (38%) experienced transient post-procedural complications, frequently of a transient renal or pulmonary nature; 1-year survival was 85%. Of patients available for follow-up computed tomography (CT), 97% (30 of 31 patients) exhibited a stable or decreasing aortic diameter and no rupture during the observational period, ненных случаях внутрибольничная летальность была значительно ниже после TEVAR (10,6%), чем после открытой операции (33,9%; p=0,002), приближая к значению выживаемости у пациентов, прошедших консервативное лечение неосложненной диссекции аорты B типа (рис. 2).

Таким образом, гraft-стентирование – привлекательная альтернатива хирургическому способу устранения ишемических осложнений (рис. 3). Зачастую закрытие при TEVAR входного отверстия расслоения на нисходящей аорте ведет к тромбозу ложного просвета и перена правлению кровяного русла в истинный просвет, за счет чего нормализуется дистальная сосудистая перфузия и восстанавливается проходимость сосудистых ответвлений [13] (рис. 4).

ПЕТТИКОАТ (Provisional Extension to Induce Complete Attachment) подход основан на идее усиления фиксирующего эффекта от стент-графта за счет дистальной установки металлического стента. Например, если мальперфузия сохраняется даже после закрытия входного отверстия ложного просвета, дополнительные стенты размещают дистально до тех пор, пока мальперфузия не будет скорректирована [14]. При таком подходе в фенестрации аорты или реваскуляризации сосудистых ответвлений с помощью непокрытых стентов нет необходимости.

Fig. 2: Comparison of medical, surgical and endovascular treatment in patients with acute type B aortic dissection [13].
Aortic Dissection

Fig. 3: Comparison of elective and emergency treated patients with type B aortic dissection [30].

justifying the conclusion that thoracic aortic stent-grafting obviously stabilized the aorta and decreased the incidence of late expansion and rupture [16]. Such observations were confirmed in a meta-analysis on patients subjected to TEVAR for of aortic dissection [17]. Procedural success was obtained in 98.2% of 609 cases with an in-hospital surgical conversion rate of 2.3% and mortality rate of 5.2%. Complications such as retrograde extension of the dissection into the ascending aorta was reported in 1.9% with neurological complications in 2.9%. Both, 30-day mortality rate and in-hospital complications were more frequent with TEVAR for acute complicated aortic dissection than in patients with chronic aortic dissections (9.8% vs. 3.2%, and 21.7% vs. 9.1% respectively; p<0.05). Interestingly, a comparison between endovascular treatment of complicated type B aortic dissection with medical therapy of uncomplicated type B dissections in 56 patients with follow-up of 18.1 ± 16.9 months reported similar outcomes in both groups with better remodelling of the descending thoracic aorta in the stent-graft group; no paraplegia and no differences in the 5-year survival rate (86.3% in both groups) were found [18].

Chronic Type B Aortic Dissection

The evolution from acute to chronic dissection involves progressive fibrosis and hardening of the intimal flap. Additionally, more intimal tears are reported in chronic versus acute type B aortic dissection. Average growth rate of chronically dissected distal aorta is estimated to range from 0.1 cm-0.74 cm per year depending on both the initial aortic diameter and the state of hypertension [19]. Unfortunately, long-term outcome of medical therapy alone is suboptimal with a reported 50% mortality at 5 years and delayed expansion of the false

ее ответвлений, т.е. случаи, рассматриваемые как осложненная диссекция аорты. Хотя долгосрочные результаты еще не получены и испытания продолжаются, технический успех был достигнут в 89% случаев, при показателе 30-дневной смертности всего 8.4% [15]. Группа пациентов из Института сердца в Аризоне (Arizona Heart Institute), состоящая из 40 человек (с диагностированной острой – 23, и хронической – 17 диссекцией аорты) получили лечение в виде TEVAR по поводу осложненной диссекции дистальной локализации. Технически успешными оказались 95% операций. Была зафиксированна одна смерть в периоперационный период, связанная с иллиакальным разрывом, а также один случай параплегии, в то время как у 15 пациентов (38%) были отмечены лишь транзиторные осложнения, часто ренальной или пульмональной природы. Выживаемость на протяжении 1 года после вмешательства составила 85%. Пациентам, по возможности, была проведена
lumen in 20%-50% patients at 4 years [1,26]. Expansion of the false lumen over 4 cm in diameter and persistent perfusion of the false lumen are considered predictors of aortic rupture and death [20,21]. There is consensus that TEVAR should be considered when aortic diameter exceeds 55-60 mm, increase of recurrent thoracic pain, or in presence of uncontrolled blood pressure and rapid growth of the dissecting aneurysm (>1 cm/year) [Fig. 5]. Nienaber et al prospectively evaluated stent-graft management in 12 patients with chronic type B dissection and compared the results with 12 matched surgical controls [22]. Proximal entry closure and complete thrombosis of the false lumen at 3 months were achieved in all patients. Stent-graft treatment resulted in no morbidity or mortality, whereas surgical treatment resulted in 4 deaths (33%; \(p=0.04\)) and 5 adverse events (42%; \(p=0.04\)) [22]. Similar results were obtained by Kato in a series of 15 patients with no mortality during a follow-up of 2 years [23]. Eggebrecht et al compared the clinical outcome of 38 patients with type B aortic dissection (10 acute and 28 chronic) after TEVAR a lower in-hospital mortality and a trend towards better 4-year survival rate in patients with chronic aortic dissection [24]. However, prophylactic implantation of stent-graft in patients with chronic type B aortic dissections was not superior to efficient medical treatment with 2 years of follow-up in the INSTEAD trial [20].

**Traumatic Aortic Dissection**

Blunt aortic injury is not infrequent and associated in 20% with motor vehicle accidents or deceleration trauma; pre-hospital mortality ranges between 80 and 90% [25]. Without appropriate treatment, 30% of survivors who reach the hospital die within the first 6 hours. Blunt thoracic aortic injury involves in 55-90% the aortic isthmus, in 10-14% the ascending aorta or aortic arch and in 15-30% the distal descending or abdominal aorta [26]. Aortic disruption is most of the time (90%) associated with other life-threatening injuries with 24% requiring major surgery before aortic repair [26]. In this scenario, with open

**Fig. 4:** (a) Malperfusion of distal aorta by occlusive type B dissection. (b) Stent-graft placement in the true lumen of the proximal descending aorta reestablished flow to the abdomen and legs.
Aortic Dissection

surgical mortality and paraplegia ranges from 54%-20%, surgery is being replaced by endoluminal stent-graft therapy with markedly lower mortality and morbidity, completely avoiding thoracotomy, single lung ventilation and heparinization [25,27]. Marcheix et al reported a primary success rate of 100% in 33 patients with aortic rupture with complete healing 1 month after TEVAR in all patients with complete reconstruction of the aortic wall and no residual pseudoaneurysm. The diameter of the aorta shrunk over the stent-graft without any signs of paraplegia during a mean follow-up of 46 months [28]. Recently, a comparative meta-analysis reviewed outcomes of 699 patients referred for endovascular or open repair surgery after traumatic aortic transsections. With a technical success rate not different from open repair (96.5% vs. 98.5%; p=0.58), TEVAR (n=370) was associated with both lower periprocedural mortality (7.6% vs. 15.2%; p=0.076) and lower incidence of paraplegia (0% vs. 5.6%; p<0.001) and stroke (0.85% vs. 5.3%; p=0.0028) [29].

On aggregate, based on the available evidence, TEVAR has become a clear therapeutic option for complicated acute distal dissection, for traumatic aortic injury with impending rupture and for selected cases of chronic dissection with emerging signs of imminent late complications.

Fig. 5: (a) Type B aortic dissection with large false lumen and compromised small true lumen. (b) Partial thrombosis of the false lumen during the chronic phase. (c) Complete thrombosis of the false lumen and re-expansion of the true lumen after stent-graft placement.
References


During the past decade arthroscopic and minimal-invasive treatment of shoulder pathologies including shoulder instabilities, acromioclavicular joint dislocations and rotator cuff tears has passed through an almost revolutionary development. Today, even complex reconstructive techniques can be performed accurately and successfully using arthroscopic techniques while preventing the disadvantages of open methods. Major advantages include a reduced morbidity, a smaller risk of infection, a better cosmetic result and a shorter rehabilitation process.

**Shoulder Instability**

Dislocation of the shoulder joint may occur after a fall on the elevated upper extremity or due to a force on the abducted and externally rotated arm, e.g. while playing football or handball or during any kind of contact sports. Pathomorphologically, a tear of the capsulolabral complex, and a posterolateral humeral head impression fracture (Hill-Sachs lesion) can result from an acute anterior shoulder dislocation. In some cases a glenoid rim fracture is observed. Conservative treatment of these injuries in active individuals often correlates with an unacceptably high recurrence rate, thus making operative stabilization the treatment of choice. Early arthroscopic capsulolabral reconstruction using suture anchors or knotless implants is a reliable fixation method, which yields good to excellent clinical results and allows a return to prior sports activity level in the majority of cases.

Chronic shoulder instabilities are characterized by recurrent dislocation events, which may lead to a loss of bony glenohumeral stability. In case of significant glenoid bone loss at the anteroinferior glenoid, soft-tissue reconstruction procedures have shown limited success rates. Open bone block procedures for glenohumeral stabilization have been used for a long time in different variations. Recently published clinical and radiological studies were able to demonstrate that an anatomical reconstruction of the glenoid concavity using a pre-shaped iliac crest autograft represents an effective fixation method. However, due to the high complexity of these procedures, they are usually performed by experienced surgeons in specialized centers.

**Neck Dislocation**

Neck dislocation of the shoulder joint may occur after a fall on the elevated upper extremity or due to a force on the abducted and externally rotated arm, e.g. while playing football or handball or during any kind of contact sports. Pathomorphologically, a tear of the capsulolabral complex, and a posterolateral humeral head impression fracture (Hill-Sachs lesion) can result from an acute anterior shoulder dislocation. In some cases a glenoid rim fracture is observed. Conservative treatment of these injuries in active individuals often correlates with an unacceptably high recurrence rate, thus making operative stabilization the treatment of choice. Early arthroscopic capsulolabral reconstruction using suture anchors or knotless implants is a reliable fixation method, which yields good to excellent clinical results and allows a return to prior sports activity level in the majority of cases.

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and durable treatment option for bony-mediated anterior shoulder instability. With the advancement of arthroscopic techniques and the development of sophisticated instruments and implants the apposition of the bone block can now be performed via an all-arthroscopic approach (Fig. 1).

**Surgical technique of arthroscopic glenoid reconstruction**

Under general anaesthesia and perioperative antibiotics the patient is placed in the lateral decubitus position. The arm and the ipsilateral iliac crest are prepped and draped in a sterile fashion. The arm is placed in 30° of abduction and 20° of external rotation with 5 kg of horizontal and 3 kg of vertical traction applied using a special arm holder. A standard posterior portal, an anteroinferior, anteroinferior and a deep anteroinferior portal are necessary to perform this procedure. A diagnostic arthroscopy is performed through the posterior portal. Concomitant lesions such as rotator cuff tears, biceps tendon pathologies or capsulolabral lesions should be addressed after the bone block apposition in order to avoid additional soft tissue swelling.

An anteroinferior working portal is created superior to the subscapularis tendon using an outside-in-technique and a Twist-In Cannula is inserted. After creating an anterosuperior viewing portal, the camera is placed anterosuperiorly using a switching stick. Hence, a second Twist-In Cannula is inserted into the posterior portal under direct visualization. The anterior and anteroinferior glenoid rim and the capsuloligamentous complex can now be evaluated thoroughly. If a significant bony defect is present, a so called “inverted-pear glenoid” can be found (Fig. 2a). The labrum is mobilized from its bed, and a capsulolabral refixation is performed using knotless anchors. The footprint of the labrum is sutured with a knotless anchor system. A diagnostic arthroscopy is performed through the posterior portal. Concomitant lesions such as rotator cuff tears, biceps tendon pathologies or capsulolabral lesions should be addressed.

Fig. 1: Schematic drawing of a large bony glenoid defect with arthroscopic reconstruction using an autologous iliac crest bone graft and a capsulolabral refixation using knotless anchors

Рис. 1: Схематическое изображение арthroскопической реконструкции крупного костного суставного дефекта, с использованием аутологичной ткани подвздошного гребня и капсуло-связочной фиксации с использованием непрерывного шва.
the glenoid neck up to the 6 o’clock position, using either a rasp or electrothermic instruments (Fig. 2b). Afterwards the glenoid rim and the scapular neck are prepped using a motorized burr to ensure adequate bony healing. Adjacent chondral defects are debrided with a shaver and, if necessary, microfractured at the end of the procedure. A deep anteroinferior portal is created through the inferior parts of the subscapularis. Another Twist-In Cannula is inserted. Next, the iliac crest bone graft is harvested. The size and the length of the graft respectively are subject to the amount of superoinferior and anteroposterior bone loss. A 2.5-3 cm x 1-1.5 cm x 1-1.5 cm tricortical bone block is harvested. After hemostasis and insertion of a drain the wound is closed in a standard fashion. Meanwhile, the graft is cleaned off soft tissue and contoured.

The arthroscope is again inserted into the gleno-humeral joint via the posterior portal. The Twist-In Cannula in the rotator interval is temporarily removed and the skin incision enlarged approximately 1 cm to allow passage of the graft. Under direct visualization the passage of the graft is dilated either with expending scissors or bluntly using the index finger of the surgeon. The pre-shaped bone block is inserted with a straight clamp and placed between scapular neck as well as the subscapularis and capsuloligamentous complex (Fig. 2c). Again, the scope is introduced in the anterosuperior portal and the Twist-In Cannula is reinserted in the anteroinferior portal using a switching stick. The incision is closed near the Cannula to avoid its loosening during further instrumentations. Now, the graft is placed anatomically at the scapular neck. The level of the bone block in relation to the glenoid surface is ensured with the aid of a switching stick introduced through the posterior portal. A significant lateral step-off has to be corrected using a burr.
after definitive graft fixation. After correct positioning of the bone block a special drill sleeve is introduced via the deep anteroinferior portal and placed at the inferior end of the graft. An integrated K-wire placement sleeve has to lie at the transition of the distal to the medial third of the bone block point superiorly. The Twist-Drill guide is pressed on to the graft and a 1.0 mm K-Wire is placed as deep as the posterior cortical wall of the scapular neck for temporary bone block fixation. Another 1.0 mm K-Wire is placed through the actual drill sleeve. To ensure parallel placement, the K-wire may be placed via the cannulated drill. If necessary, a 1.6 mm K-wire can be placed via the anteroinferior portal or percutaneously to guarantee rotational stability of the bone block. The inferior K-wire is overdrilled using a cannulated drill under direct visualization. Next, the thread cutter is inserted manually over the K-wire. The K-wire is removed, the first Bio-Compression Screw is inserted and placed 1-2 mm below the glenoid level. The Twist-Drill Guide is now rotated 180° clockwise (right shoulder) or counterclockwise (left shoulder) with the first K-wire remaining in the K-wire placement sleeve as a rotational center. The second drill hole is placed parallel and superior to the first one in the same way and the second Bio-Compression Screw can be inserted parallel to the first one. The graft surface can be smoothed with a shaver and, if necessary, a lateral step-off may be removed and the bone block made level with the glenoid surface. Next, the anteroinferior labrum is reattached to the original glenoid rim using a knotless anchor. Two additional knotless anchors are used for reconstruction of the anteroinferior labrum, so that the anterior part of the graft is partly covered (Fig. 2d). Finally, other accompanying lesions such as chondral defects, rotator cuff tears, biceps tendon pathologies or HAGL-lesions can be addressed. Finally, the arthroscopic portals are closed in a standard fashion.

In our department performed mid-term follow-up studies of this anatomic arthroscopic reconstruction technique show that and for the graft to be transferred, the utilization of a temporary bone block fixator. The inferior portal or percutaneously can be placed via the anteroinferior portal and placed at the inferior end of the graft. A special drill sleeve is inserted and removed, the first Bio-Compression Screw can be inserted and removed, the second Bio-Compression Screw can be inserted parallel to the first one. The graft surface can be smoothed with a shaver and, if necessary, a lateral step-off may be removed and the bone block is made level with the glenoid surface. Next, the anteroinferior labrum is reattached to the original glenoid rim using a knotless anchor. Two additional knotless anchors are used for reconstruction of the anteroinferior labrum, so that the anterior part of the graft is partly covered (Fig. 2d). Finally, other accompanying lesions such as chondral defects, rotator cuff tears, biceps tendon pathologies or HAGL-lesions can be addressed. Finally, the arthroscopic portals are closed in a standard fashion.

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promising results in restoring the stability of the shoulder joint while preserving the integrity of the subscapularis tendon.

**Acromioclavicular Joint Instability**

Acromioclavicular joint dislocations are one of the most common injuries of the shoulder girdle, especially in young and active patient population. Typically, these injuries result from a direct fall on the shoulder, e.g. during a bike accident, leading to a depression of the scapula relatively to the clavicle. Recently, arthroscopically-assisted techniques, that reestablish the anatomy and stability of the AC-joint using pulley-like implants, have been developed for the treatment of acromioclavicular joint instabilities (Fig. 3).

**Surgical technique of arthroscopic AC-joint reconstruction**

The procedure is performed under general anaesthesia and perioperative antibiotics the patient is placed in the beach-chair position with the ipsilateral arm and shoulder prepped and draped in a sterile fashion. In addition to a two centimeter incision on top of the clavicle, a posterior and lateral viewing portal and an anteroinferior working portal are used for this procedure. A diagnostic arthroscopy is performed via the standard posterior portal. In cases of gleno-humeral concomitant lesions those are treated first. After the diagnostic arthroscopy, an anteroinferior working portal just above the subscapularis tendon as well as a transdinous lateral viewing portal approximately one centimeter posterior to the anterior border of the supraspinatus tendon are hence established using the outside-in technique. The incision of the lateral viewing portal is made parallel to the tendon fibres of the supraspinatus and the deltoid in order to minimize the trauma of access. A two centimeter sagittal incision is made over the clavicle approximately three cm from the lateral border of the clavicle to expose the undersurfaces of the undersurface of the coracoid arch after placement of the first transclavicular-transcoracoidal K-wire (4a), overdrilling and insertion of a nitinol suture passer via the drill (4b), placement of the second tunnel (4c) and finally the insertion and orientation of the inferior buttons of the pulley-like implants (4d).

**Fig. 4a-d: arthroscopic view via the anterolateral portal showing the undersurface of the coracoid arch after placement of the first transclavicular-transcoracoidal K-wire (4a), overdrilling and insertion of a nitinol suture passer via the drill (4b), placement of the second tunnel (4c) and finally the insertion and orientation of the inferior buttons of the pulley-like implants (4d).**

**Рис. 4: Артроскопический вид через передне-боковой доступ нижней поверхности клювовидного отростка лопатки после чресключично-клювовидного размещения спицы Киршнера (a), просверливание и введение проводника через просверленный канал (b), расположение второго туннеля (c) и окончательное введение и размещение нижней части имплантанта типа шкива (роликового блока) (d).**

**Повреждения акромиально-ключичного сочленения**

Вывихи акромиально-ключичного сустава (сочленения) – одна из наиболее часто встречающихся травм, особенно среди молодых и активных пациентов. В типичных случаях такое повреждение возникает в результате прямого падения на плечо, включая падение с велосипеда, приводящее к смещению лопатки относительно ключицы. В последнее время, были разработаны эффективные артроскопические техники восстановления анатомической целостности и стабильности акромиально-ключичного сустава с использованием имплантантов, сконструированных как роликовый блок (шлиф) (рис. 3).

**Хирургические техники артроскопической реконструкции акромиально-ключичного сустава**

Процедуру проводят под общей анестезией, с предварительным предоперационным введением антибиотиков. Пациента помещают в специальное кресло-шезлонг, подготавливая исцелительные руку и плечо, обкладывая их стерильными пеленками. В дополнение к этому делают сантиметровый разрез.
centimeters medial to the AC joint. With the aid of a small periosteal elevator the superior surface of the clavicle is cleared off soft tissue. Using a switching stick the arthroscope is then introduced through the anteriorinferior portal. Now, the subcoracoidal space and the base of the coracoid are prepped with the aid of a radiofrequency ablation device or a shaver introduced through the anteroinferior portal. The aim is to obtain a clear visualisation of the undersurface of the coracoid arch through which the drill holes are to be made. Therefore an anterior cruciate ligament drill guide and marking hook is introduced through the anteroinferior portal under direct visualization and placed under the medial part of the coracoid while its other end (the drill sleeve) is placed over the desired entry point about 4.5 cm from the lateral end of the clavicle. An image intensifier is used in all cases for the correct placement of the drill holes and reduction of the AC joint. The first oblique drill hole (transclavicular-transcoracoidal) is made from superomedial in line of the previous conoid ligament. With the drill guide held in this position and under a clear arthroscopic view of the marking hook, a 2.0 mm K-wire is drilled through the clavicle and the base of the coracoids (Fig. 4a). The K-wire is overdrilled using a cannulated drill bit (4.0 mm) after which a nitinol suture passer is inserted into the subcoracoidal space through the drill (Fig. 4b). The nitinol wire is retrieved via the anteroinferior portal. The cannulated drill bit is then removed and both ends of the nitinol suture passing wire are held with a clamp. The second transclavicular-transcoracoidal drill hole in line of the trapezoid ligament is established approximately 2 cm lateral to the first one in a similar fashion (Fig. 4c). After overdrilling of the K-wire the nitinol suture passer is introduced and retrieved via the anteroinferior portal. Now the two pulley-like implants (i.e. Tight-Rope, Arthrex, Fl, USA) are attached to each nitinol suture passer and pulled from the other end under arthroscopic control until the oval shaped button is flipped beneath the coracoid arch. A grasper is used to place both

Рис. 5: Послеоперационная рентгенограмма демонстрирует финальные результаты артроскопической реконструкции акромиально-ключичного сочленения методом двойного Tight-Rope.
inferior buttons parallel to each other and perpendicular to the coracoid base (Figure 4d). Now the assistant supports the weight of the arm and the surgeon pulls on the No. 5 Fiber-wire sutures of the Tight-Rope devices thereby reducing the AC joint anatomically under x-ray control. In order to ensure that both TightRopes are under equal tension this is performed by alternating the pull between the two devices. Once reduction is achieved the medial sutures are knotted first followed by the lateral ones. The arthroscopic portals are closed in a standard fashion. Postoperatively radiographs are taken (Fig. 5).

In our hands this combined arthroscopically assisted and image intensifier controlled double TightRope technique using implants of the first generation represents a safe technique and yields good to excellent clinical results despite the presence of partial recurrent vertical and horizontal AC joint instability. Short- and medium term clinical and radiologic results of modern arthroscopic methods are at the least comparable to open techniques. Here, a second surgical intervention for implant removal is not obligatory.

Rotator Cuff Tears:
The spectrum of rotator cuff injuries ranges from so-called partial defects to massive tears of several tendons. The inability to center the humeral head in the glenoid fossa can lead to physical symptoms like pain, weakness, decreased range of motion and sometimes instability. Symptomatic smaller defects usually produce pain with overhead activities, whereas massive tears may lead to a functional deficit. Both small partial defects as well as large or massive complete tears of the rotator cuff are today a domain of arthroscopic surgery. In early days, arthroscopic single-row repair was considered the standard technique.

Fig. 6: Schematic drawing of a knotless double row supraspinatus tendon reconstruction.

Рис. 6: Схематическое изображение проведения реконструкции надостного сухожилия двухрядным непрерывным швом.
for rotator cuff repair. More recently, double-row repairs were introduced. The potential benefit of the latter technique represents the enlarged footprint coverage, a more solid fixation due to better force distribution and an increased initial fixation strength which eventually should lead to superior clinical and radiological results. With the advancements of double-row repairs even knotless tendon reconstruction techniques have been developed which are supposed to better distribute pressure to the tissues underneath, hence, reducing tendon damage compared to classic double-row repairs (Fig. 6).

Surgical technique of arthroscopic knotless double-row supraspinatus tendon repair

The surgical procedure is performed with the patient in the beach-chair position under general anaesthesia. Preoperatively intravenous antibiotics are administered. Routine portals are used. A diagnostic arthroscopy via a standard posterior portal is performed. In cases of biceps tendon pathology a biceps tenotomy or tenodesis is performed first. The supraspinatus tendon defect is evaluated via the posterior portal (Fig. 7a). After debridement of the cuff and the greater tuberosity two knotless anchors with lace-like sutures (Fiber-Tape, Arthrex, Fl, USA) are inserted via the anterolateral and the lateral portals (Fig. 7b). The arthroscope is now switched into the subacromial space via a posterolateral portal. The sutures are passed through the tendon using different penetration devices in a mattress stitch configuration (Fig. 7c). Afterwards the anterior limb of the Fiber-Tape of the anterior and the posterior anchor are retrieved laterally, brought under slight tension and fixed with another knotless anchor distal to the tip of the greater tuberosity without knot-tying. The same procedure is repeated with the posterior limb of the and horizontal acromial-bursal instability. Clinical and radiological results are comparable with those of shorter and longer-term follow-ups. New arthroscopic techniques which are used to fix the cuff have shown promising results in clinical and radiological tests. In combination with a primary fixation they are able to produce better clinical and radiological results. Improved fixation techniques are developed which are supposed to distribute pressure to the tissues underneath, hence, reducing tendon damage compared to classic techniques.

Fig. 7a-d: Arthroscopic view via the posterior portal showing a supraspinatus tendon tear (7a), placement of knotless anchors with Fiber-Tapes (Arthrex, Fl, USA) attached into the greater tuberosity (7b), suture penetration of the supraspinatus tendon (7c) and the final repair after double row knotless tendon reconstruction (7d).
Shoulder Surgery

Conclusion
Arthroscopic and minimal-invasive treatment strategies of shoulder instabilities, acromioclavicular joint dislocations and rotator cuff tears have shown a tremendous development during the last decade. Although, most of the modern procedure still have to stand the test of time in long-term follow-up studies. However, the short- and midterm results have shown that even complex reconstructive techniques can be performed accurately and successfully using arthroscopic techniques preventing the disadvantages of traditional open methods.

Хирургическая техника артроскопической реконструкции надостного сухожилия непрерывным двухрядным швом
Пациента располагают в кресле-щелонге, проводят общую анестезию. Предварительно проводят курс антибиотиков. Используют обычные доступы. Диагностическую артроскопию проводят через передний доступ. В случаях патологии бицепса в первую очередь проводят тенотомию или тенодезис. Для восстановления повреждений надостного сухожилия используют задний доступ (рис. 7, а). После санации манжеты и большой бугристости два гладких фиксатора с кружевоподобным шовным материалом (Fiber-Tape, Arthrex, Fl, USA) вводят через передне-боковой или боковой доступы (рис. 7, б). Артроскоп переводят в субакромиальное пространство посредством задне-бокового доступа и прошивают сухожилия матрасным швом (рис. 7, в). После чего передний конец нити (Fiber-Tape) переднего и заднего фиксатора возвращают латерально, прошивая с небольшим усилием и закрепляют его, соединяют с другим дистальным фиксатором, и, не прерывая, присоединяют его к верхушке большой бугристости. Такую же процедуру повторяют для задней и передней фиксации; таким образом, задний фиксатор образует мостоподобную конструкцию на верхушке восстановляемого сухожилия (рис. 7, д). Затем, при наличии показаний, проводят субакромиальную декомпрессию.

Исходя из данных опубликованных за последнее время клинических исследований, нельзя выделить какой-либо из методов как наиболее эффективный.

Доступные радиографические наблюдения показали значительные потенциальные преимущества восстановления структурной целостности вращательной манжеты с помощью двухрядного непрерывного шва у пациентов с повторным повреждением, а также более низкий уровень нежелательных послеоперационных симптомов.

Выводы
Артроскопические и миниминвазивные методы лечения нестабильности плечевого сустава, вывихов акромиально-ключичного сочленения, повреждения ротационной манжеты существенно развились за последнее время. Кроме того, большинство современных операций до сих пор проходят клинические испытания для выявления долгосрочных последствий их проведения. Как бы там ни было, краткосрочные и средние результаты показали, что даже сложные реконструктивные операции могут быть выполнены точно и успешно благодаря артроскопическим методикам, позволяющим предотвратить неблагоприятные последствия открытых хирургических вмешательств.
References:


Hobby J, Griffin D, Dunbar M, Boileau P. Is arthroscopic surgery for stabilisation of chronic shoulder instability as effective as open surgery? JBJJS 2007;89-B:1188-96.


Scheibel M, Kraus N. Arthroscopic reconstruction of the glenoid concavity with an autologous bone block procedure. Orthopade 2010;40:52-60. German.


Treatment of Hilar Cholangiocarcinoma from the Surgeon’s Perspective

Introduction
The presence of a primary malignant tumour of the bile duct was first described by Durand-Fardel in 1840. The term Klatskin tumour was defined later when a tumour was located at the confluence of the hepatic bile ducts, as reported by Gerald Klatskin in 1965. Cholangiocarcinomas are rare tumours, although in recent years there has been an increased incidence of 3–4 new cases per 100,000 people (Khan, Heimbach et al. 2005). Bile duct cancer accounts for about 2% of all malignant tumours and are thus the fifth most common tumour of the gastrointestinal tract.

Well into the 1970’s, central cholangiocarcinomas were considered to be non-resectable, making palliative care the only available treatment option at that time. Only in the last three decades have invasive surgical procedures for tumour resection superseded the purely palliative approach, thereby allowing for potentially curative treatment (Lang, Kaiser et al. 2006). Even today, curative treatment is only accomplished in roughly 30% of all patients. This is why palliative care continues to be of central importance to the majority of patients.

Diagnostics and Pathology
Clinical staging should include contrast-enhanced computed tomography (CT) or magnetic resonance imaging (MRI) of the abdomen as well as a thoracic CT. Magnetic resonance cholangiography (MRC) is also frequently discussed as a gold standard (Romaneehsen, Otto, et al. 2004). Combined PET/CT is particularly useful for excluding distant metastases, detecting the primary tumour and monitoring treatment. Currently, PET/CT is an auxiliary examination technique used in studies for extended staging, and is also being investigated by our working group in animal and clinical trials (Li, Kuehl et al. 2008).

So far, primary staging for hilar bile duct cancer has only provided very limited insight into the actual stage of tumour progression. Also at our own centre, 10% of all cases in which surgery was performed
for suspected malignant biliary stenosis are during histological examination ultimately revealed to be benign growths, referred to as Klatskin-mimicking lesions (Juntermanns, Kaiser et al. 2011).

According to the Klatskin tumour analysis of the Essen database, the tumour marker Ca 19-9 is a useful tool for preoperative evaluation of resectability (Juntermanns, Radunz, et al. 2010). If this marker is highly elevated (>1000 U/ml), the rate of resectable tumours drops to 30% in comparison to patients with slightly or moderately elevated tumour markers. Moreover, the tumour marker level is also significantly correlated with the UICC tumour stage.

Carcinomas rapidly grow into the surrounding connective tissue of the hepatoduodenal ligament and continue to progress into the liver. Depending on tumour local spread, about half of all patients already have regional lymph node metastases at the time of diagnosis, and are thus at an advanced tumour stage when treatment is initiated. More than 80% of patients are already showing perineural invasion when the diagnosis is made. Haematogenous distant metastases occur comparatively late. Intrahepatic or peritoneal metastases, however, arise far earlier and much more frequently (Tannapfel, Wittekind 2004).

The identified statistically significant indicators of Klatskin tumours were tumour size including the extent of local invasion, presence of lymph node metastases, distant metastases, the UICC stage and tumour-free resection edges (Lang, Kaiser et al. 2006).

A conclusive evaluation of the tumour stage according to UICC (Union Internationale Contre le Cancer) can only be made once all clinical results including imaging, the surgeon’s assessment and the pathologist’s findings are available. In the patients, in which was performed surgery due to the suspicion of a malignant biliary stenosis, histological examination ultimately revealed to be benign growths, referred to as Klatskin-mimicking lesions (Juntermanns, Kaiser et al. 2011).

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This complicates stage-appropriate treatment, particularly in terms of neoadjuvant therapy protocols.

**Prognosis and Therapeutic Concepts**

The only potentially curative treatment option is complete tumour resection (R0 resection) including bile duct resection and hemihepatectomy, or a liver transplant following hepatectomy (Kaiser, Sotiropoulos, et al. 2010).

Despite considerable progress in the surgical treatment of hilar cholangiocarcinoma, its prognosis is still not satisfactory. Even after curative tumour resection, the 5-year survival rate is only 23% to 46% and a mere 9% to 34% if a tumour has been microscopically detected at the resection edge (Lang, Kaiser et al. 2006). The prognosis for patients is poor since the central location of tumours in the porta hepatis only allows for very smalls safety margins, and because cholangiocarcinoma characteristically expand in a discontinuous fashion. The current surgical standard for the treatment of cholangiocarcinoma involves the complete resection of extra-hepatic bile ducts, starting from the duodenum including the bile duct bifurcation with regional lymphadenectomy as well as hemihepatectomy.

In patients with healthy livers, approx. 70-75% of functional hepatic tissue can be resected, depending on the patient’s age, without causing the risk of severe post-operative liver insufficiency [5]. However, the majority of cholangiocarcinoma patients have pre-existing obeselowanie, включая методы визуализации, осмотр хирурга и изучены результаты гистологии, что усложняет лечение, особенно в отношении протоколов неoadъювантной терапии.

**Прогноз и концепция терапии**

Единственным потенциально курабельным методом лечения является полная резекция опухоли (резекция R0), включая резекцию желчного протока, и гемигепатэктомия, или пересадка печени после гепатэктомии (Kaiser, Sotiropoulos c соавт., 2010). Несмотря на значительный прогресс в хирургическом лечении холангиокарциномы ворот печени, прогноз заболевания остается неудовлетворительным.

Даже после радикальной резекции опухоли выживаемость в течение 5 лет составляет всего от 23 до 46%, и лишь от 9 до 34%, если опухоль была обнаружена микроскопически в области края резекции (Lang, Kaiser с соавт., 2006). Особенно неблагоприятный прогноз у пациентов с расположением опухоли в области ворот печени, что обусловливает очень небольшое безопасное расстояние до края резекции, и, соответственно, дальнейший быстрый рост холангиокарциномы.

В настоящее время стандарт хирургического лечения холангиокарциномы включает полную резекцию экстрапеченочных желчных протоков, начиная с двенадцатиперстной кишки, в том числе бифуркации общего желчного протока с региональной лимфаденэктомией, а также гемигепатэктомией.

У пациентов со здоровой печенью можно рекомендовать приблизительно 70–75% функциональной ткани печени, в зависимости от
liver damage. This is due to a multitude of causes, including cholestasis, fibrosis, cirrhosis or hepatic steatosis.

After exploration of the abdomen, resectability is assessed. In case of local inoperability or uncertainty about whether or not a R0 resection can be performed, transplantation is considered as possible treatment option. Liver transplantation allows for complete removal of the tumour with the necessary safety margin enabled by heptectomy and central bile duct resection, also for locally expanded conditions that could not even be treated successfully with an extended liver resection.

Surgical procedure for a resectable tumour: Severing the common bile duct at the upper edge of the pancreas including the remaining lymphatic channels and lymph nodes up to the upper edge of the pancreas. Subsequently, the entire bile duct tissue is resected. Lymph node dissection at the proper hepatic artery and common hepatic artery up to the celiac artery; the hepatic portal vein and, possibly, an accessory hepatic artery of mesenteric artery are exposed. En-bloc resection of the cholangiocarcinoma by means of heptectomy; the distal resection edge is examined using the frozen section technique; second resection, if necessary. The biliary flow and the remaining liver tissue is reconstructed using Roux-en-Y hepaticojejunostomy.

If bilateral hepatic, vascular or pancreatic invasion is present, a complete tumour resection is often not possible, making palliative care the only treatment option, as is the case with distant metastases. In individual cases, it may, however, still be possible to remove all tumour tissue by means of extensive resections including complex vascular reconstruction and pancreatic resection.

For patients who are no longer eligible for curative therapy, a biliary drainage is of central importance. After surgical treatment of a non-resectable Klatskin tumour, the median survival time is 6-16 months, возраста пациента, не вызывая при этом риск развития тяжелой послеоперационной печеночной недостаточности. Однако у большинства пациентов с холангиокарциномой уже существуют вреждения печени. Это связано со множеством причин, включая холестаз, фиброз, цирроз или стеатоз печени.

После исследования брюшной полости оценивается реекстабельность. В случае неоперабельности или невозможности проведения R0 резекции возможным вариантом лечения считается трансплантация печени.

Трансплантация печени позволяет полностью удалить опухоль и центральный желчный проток с обеспечением противоопухолевой безопасности (безопасным расстоянием от опухоли до края резекции), а также при таком локальном распространении опухоли, которое может быть вылечено с помощью расширенной резекции печени.

Хирургическое вмешательство при резектабельности опухоли: иссечение общего желчного протока у верхнего края поджелудочной железы, в том числе остатьсяших лимфатических протоков и лимфатических узлов, до верхнего края поджелудочной железы. Далее иссекают всю ткань желчного протока.

Выполняется иссечение лимфоузлов на собственной печеночной и общей печеночной артерии до чревной артерии; на печеночной воротной вене и, возможно, добавочной печеночной артерии из брыжеечной артерии.

Резекция выполняется «единым блоком» путем гемигепатэктомии; дистальный край резекции исследуется с использованием метода замораживания срезов, при необходимости проводится еще одна резекция. Желочные протоки и оставшиеся ткани печени восстанавливаются путем гепатикоэуностомии по Ру.

В случае двустороннего поражения печени, сосудов и поджелудочной железы полное удаление опухоли часто не представляется возможным, что делает паллиативную помощь единственным вариантом лечения, как и в случае с отдаленными метастазами. В отдельных случаях однако, возможно удаление всей опухолевой ткани с помощью
From a palliative point of view, hepaticojejunostomy, or hepaticojejunostomy of the segments III and V for complete blockage of the central bile ducts, may represent an alternative to avoid intermittent endoscopic or percutaneous biliary stenting (Kaiser, Frühauf et al. 2008). The median survival time after intermittent stenting within palliative care was 3-8 months. Nevertheless, repeated application of endoscopic photodynamic therapy has a high response rate and made it possible to significantly extend survival from 7 to 21 months in comparison to the control group (Zoepf, Jakobs et al., 2005). At least in palliative care, photodynamic therapy is showing promise, although its benefits still need to be examined in larger randomised studies.

Furthermore, intraoperative, intraductal and external radiation as well as systemic chemotherapy represent treatment options in palliative care. The results of current neoadjuvant and adjuvant therapy are unsatisfactory in both palliative care and curative treatment with complete tumour resection. Nevertheless, a randomised multicentre study this year showed a significant survival advantage for patients who received a combination therapy with Cisplatin and Gemcitabine (Valle, Wasan et al. 2010). More recent cancer therapy approaches, which include biologicals such as inhibitors of the vascular endothelial growth factor (VEGF), appear to be highly promising both in-vitro and in small case series (Wiedmann, Mössner 2010).

The aim of modern radiation techniques involving intraoperative radiation therapy, stereotactic 3D radiation therapy or future proton therapy is to achieve an extensive resection with a complex reconstruction of the ducts and therafted bile ducts. The current neoadjuvant and adjuvant therapy are not satisfactory in both palliative care and curative treatment with complete tumour resection.

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Table 2: 2009 TNM classification (7th edition)

<table>
<thead>
<tr>
<th>T primary tumour:</th>
<th>2009 TNM classification (7th edition)</th>
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<tbody>
<tr>
<td>• T1 Tumour limited to bile duct</td>
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<tr>
<td>• T2a Tumour invading neighbouring soft tissues</td>
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<tr>
<td>• T2b Tumour invading hepatic parenchyma</td>
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<tr>
<td>• T3 Tumour invading unilateral branches of the hepatic portal vein or the common hepatic artery</td>
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<tr>
<td>• T4 Tumour invading main branch/ bilaterally of hepatic portal vein / common hepatic artery and hepatic bile duct</td>
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<table>
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<th>N regional lymph nodes:</th>
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<tr>
<td>• NX Regional lymph nodes can not be evaluated</td>
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</tr>
<tr>
<td>• N0 No regional lymph node metastases</td>
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<tr>
<td>• N1 Regional lymph node metastases (cystic duct / common bile duct, common hepatic artery and hepatic portal vein)</td>
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<th>M distant metastases:</th>
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<tbody>
<tr>
<td>• M0 No distant metastases</td>
<td></td>
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<tr>
<td>• M1 Distant metastases</td>
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For patients, whom cannot received radical therapy, the combination therapy with Cisplatin and Gemcitabine (Valle, Wasan et al. 2010). More recent cancer therapy approaches, which include biologicals such as inhibitors of the vascular endothelial growth factor (VEGF), appear to be highly promising both in-vitro and in small case series (Wiedmann, Mössner 2010).

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intensify local tumour treatment while protecting the surrounding tissue as much as possible. Healthy tissue of the gastrointestinal tract located in or near the irradiated area remains largely untouched by the radiation volume, thus protecting it from potential radiation damage. In our experience, intraoperative radiation of Klatskin tumours can considerably extend the survival of patients, especially within palliative care (Kaiser, Frühauf et al. 2008).

If the prognosis for patients with central cholangiocarcinoma continues to be poor, the optimisation of multi-modal therapeutic concepts for palliative and curative treatment is required. Highly promising data has been provided by the Mayo Clinic in Rochester (U.S.), for example. 5-year survival rates of up to 82% have been reported following liver transplantation after completion of a neoadjuvant treatment regimen including radio chemotherapy (Rosen, Heimbach, et al. 2010).

Prospects
As a centre for hepatobiliary surgery in Germany, the University Hospital of Essen is highly involved in the treatment of Klatskin tumours compared to other hospitals. In combination with the University Hospital of Essen, we are offering a comprehensive treatment concept for patients with Klatskin tumours. The concept includes local therapy options such as radiofrequency ablation, cryoablation, and percutaneous alcohol injection, as well as systemic treatment options such as chemotherapy and targeted therapy. In addition, we are continuously improving our surgical techniques to achieve optimal oncological and functional results.

Tumour Follow-up Care
Tumour follow-up care is provided every three months during the first year, every six months during the second year and thereafter annually. It requires the following examinations:
• Anamnesis and physical examination
• Routine lab and tumour marker monitoring
• Chest radiograph and abdominal CT
Optionally: MRCP, thoracic CT and PET-CT

Neoadjuvant radio chemotherapy
Liver transplantation

Discussing the individual case in an oncological / surgical conference as well as in a liver transplantation conference

Exploratory laparotomy and lymphadenectomy for tumours which are locally non-resectable without transplantation

Table 3a: Schematic overview of the “Essen Treatment Protocol” for transplantation patients with locally resectable tumours without metastases
Hilar Cholangiocarcinoma

Table 3b: Schematic overview of the “Essen Treatment Protocol” for patients with locally resectable tumours without metastases

<table>
<thead>
<tr>
<th>Schematic Overview of the “Essen Treatment Protocol” for Patients with Locally Resectable Tumours without Metastases</th>
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<tbody>
<tr>
<td><strong>All eligible and consenting patients with central cholangiocarcinoma</strong></td>
</tr>
<tr>
<td>3. Histological diagnosis using ERCP; Alternatively, proof provided by high tumour markers</td>
</tr>
<tr>
<td>4. Excluding distant metastases in PET-CT</td>
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<tr>
<td>→ Discussing the individual case in an oncological / surgical conference</td>
</tr>
<tr>
<td><strong>Central bile duct resection with hemihepatectomy and lymphadenectomy for locally resectable tumours</strong></td>
</tr>
<tr>
<td>→ Discussing the individual case in an oncological / surgical conference</td>
</tr>
<tr>
<td><strong>Adjuvant radio chemotherapy only for incomplete tumour resection (R1) or metastases in final histology</strong></td>
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</table>

From our point of view, an exploratory laparotomy performed by an experienced surgeon is indicated for all eligible patients without preoperatively diagnosed distant metastases. For a highly selective group of patients, the removal of the entire liver (hepatectomy) together with the extra-hepatic bile duct and a subsequent liver transplantation represents an available procedure. Especially patients with locally spread tumours, which are not fully resectable without transplantation, have a chance of long-term survival with a liver transplant. Adjuvant oncological treatment and radiation therapy can additionally help improve the patients’ prognosis.

Table 3b: Схематический обзор «Протокол лечения ESSEN» для пациентов с резектабельными опухолями без метастазов

Последующее лечение и наблюдение
Долечивание опухоли осуществляется каждые три месяца в течение первого года, каждые шесть месяцев в течение второго года и далее ежегодно. Это требует следующих исследований:
• Сбор анамнеза и физикальное обследование.
• Обычные лабораторные исследования, уровень опухолевого маркера.
• Рентгенограмма грудной клетки и КТ брюшной полости.
• МРТ, КТ грудной клетки и ПЭТ-КТ.

Дополнительно: МРТ, КТ грудной клетки и ПЭТ-КТ.

Перспективы
Как центр гепатобилиарной хирургии в Германии, клиника Университета Эссена больше других больниц занимается лечением опухоли Клацкина. Располагая современной лучевой терапией и онкологией, опухолевый центр в Эссене обеспечивает оптимальные условия для лечения холангиокарциномы и даже для трансплантации печени.

С нашей точки зрения, диагностическая лапаротомия, которая выполняется опытным хирургом, показана для всех пациентов без отдаленных метастазов. Для избирательной группы пациентов удаление всей печени является реалистичной процедурой. Они не являются полностью резектабельными без пересадки, получают серьезный шанс на выживание в долгосрочной перспективе после пересадки печени. Адъювантная и лучевая терапия могут дополнительно улучшить прогноз.
### Literature


### Table 3c: Schematic overview of the “Essen Treatment Protocol” for patients with non-resectable tumours or metastases

<table>
<thead>
<tr>
<th>Step</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.</td>
<td>All eligible and consenting patients with central cholangiocarcinoma</td>
</tr>
<tr>
<td>2.</td>
<td>Histological diagnosis using ERCP; Alternatively, proof provided by high tumour markers</td>
</tr>
<tr>
<td>3.</td>
<td>Excluding distant metastases in PET-CT</td>
</tr>
<tr>
<td>4.</td>
<td>Exploratory laparotomy for locally non-resectable tumours and/or distant metastases</td>
</tr>
<tr>
<td>5.</td>
<td>Discussing the individual case in an oncological / surgical conference</td>
</tr>
<tr>
<td>6.</td>
<td>Palliative care including chemotherapy / radio chemotherapy / photodynamic therapy</td>
</tr>
</tbody>
</table>

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Therapeutic Standards in Colon Cancer

Introduction

Epidemiology and Etiology

Colorectal cancers occur in approximately 8.1 million people per year worldwide. Over the past 20 years, there has been an overall decrease in the incidence of colon cancer which is mainly attributed to improved screening and prevention. According to the presence or absence of inherited or familial predispositions for colorectal cancer, three types of colorectal cancer are distinguished:

1. Inherited disorders with strongly increased risk for colon cancers account for less than 5% of colon cancer cases. These known inherited disorders are subdivided according to the presence or absence of multiple colonic polyps into inherited polyposis syndromes with hundreds to thousands of colon and rectal polyps (FAP = familial adenomatous polyposis) and inherited colon cancer without multiple colonic polyps (HNPCC = hereditary non-polyposis colorectal cancer = Lynch-syndrome). FAP is an autosomal dominant disease with a 100% life-time-risk for colorectal cancer caused by mutations in the APC gene and accounts for less than 1% of all colorectal carcinomas. HNPCC accounts for about 2-3% of all colorectal cancers, originates from mutations in one of several DNA mismatch repair genes causing microsatellite instability (MSI) and results in a 50% life-time-risk for colorectal cancer.

2. About 20% of the patients with colorectal cancer have a positive family history for colorectal cancer. The exact genetic reasons for these familial accumulations of colorectal cancer cases are still unknown.

3. Colorectal cancers occurring in patients without any detectable familial or inherited predispositions are called sporadic and account for about 75%-80% of all colorectal carcinoma cases. It is well understood that the development of sporadic colon cancer is a multistep process of genetic mutations which drives the transformation from normal colonic epithelium over dysplasia to invasive cancer (adenoma-carcinoma-sequence: Vogelstein-model). While the exact...
causes for developing sporadic colon cancer have not been completely elucidated yet, a number of risk factors are identified that are associated with an increased risk for colon cancer (Table 1).

Polyp
The word “polyp” refers to a macroscopically visible lesion or mass projecting from an epithelial surface. Polyps may be classified as neoplastic or non-neoplastic. Neoplastic polyps are epithelial tumors such as adenomas, adenocarcinomas, and carcinoid tumors, as well as non-epithelial lesions such as lipomas, leiomyomas, and lymphomatous polyps. Non-neoplastic polyps include hamartomas, hyperplastic polyps, and inflammatory polyps. The adenoma, a benign neoplasm of the epithelium, is the most common and most important colorectal polyp. Most adenocarcinomas arise from adenomas, and the removal of adenomas by colonoscopy or by combined laparoscopic-endoscopic techniques has been shown to be effective in decreasing the incidence of colorectal cancer. When an adenoma or adenocarcinoma is found, every effort should be made for a complete colonoscopy to the coecum because of the high rate of synchronous neoplasms.

Screening and Prevention
Colon cancers usually progress through the above mentioned adenoma-carcinoma-sequence from benign adenomas to invasive cancer over five to ten years, which represents the rationale for screening programs. This transformation process over years provides the opportunity to prevent cancer by removing these polyps prior to the onset of cancer. Colonoscopy is the gold standard for screening and prevention of colon cancer.

Table 1: Factors with increased risk for colon cancer
Таблица 1: Факторы риска возникновения колоректального рака

<table>
<thead>
<tr>
<th>Risk category</th>
<th>Screening recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Average (no risk factors as below)</td>
<td>Colonoscopy beginning at age 50, repeated every 10 years if no polyps (adenomas) are present</td>
</tr>
<tr>
<td>Inflammatory bowel disease</td>
<td>Colonoscopy beginning 8-10 years after onset of IBD-symptoms, repeated every 1-2 years</td>
</tr>
<tr>
<td>Positive family history (one first-degree or two second-degree relatives with colorectal cancer any age)</td>
<td>Colonoscopy beginning at age 40 or 10 years prior to earliest colorectal cancer in family</td>
</tr>
<tr>
<td>HNPCC</td>
<td>Colonoscopy beginning at age 25, repeated every year</td>
</tr>
<tr>
<td>FAP</td>
<td>Colonoscopy beginning at age 10, repeated every year</td>
</tr>
</tbody>
</table>

Table 2: Screening recommendations for colorectal cancer
Таблица 2: Скрининг-рекомендации для колоректального рака

Screening and Prevention
Colon cancers usually progress through the above mentioned adenoma-carcinoma-sequence from benign adenomas to invasive cancer over five to ten years, which represents the rationale for screening programs. This transformation process over years provides the opportunity to prevent cancer by removing these polyps prior to the onset of cancer. Colonoscopy is the gold standard for screening and prevention of colon cancer.
Only colonoscopy can verify a colon cancer by taking biopsies for histological evaluation and only colonoscopy can both detect and remove colonic polyps as possible precursors of colon cancer making routine cancer prevention effective.

Table 2 gives recommendations for colon cancer screening (Table 2).

Clinical Staging
Once the diagnosis of colon cancer is histologically confirmed, clinical staging is important to determine the local extent of the primary tumor and the presence or absence of distant metastases. It routinely comprises physical examination including digital rectal examination, colonoscopy, ultrasound or CT scan of the abdomen and chest X-ray (Fig. 1).

In special cases, additional diagnostics might be necessary with magnetic resonance imaging (MRI), positron emissions tomography (PET) or virtual colonoscopy (CT- or MRI-colonography) (Fig. 2).

The staging of colorectal cancer assesses the depth of penetration of the bowel wall, the involvement of regional lymph nodes, the involvement of adjacent organs, and the presence or absence of distant metastases.
Moreover, a functional evaluation of the general health and organ functions of the patient by experienced medical staff is inevitable to weight the possible risks and benefits of the treatment options (Fig. 3).

Surgery
The mainstay therapy for colon cancer and the only treatment option, which can result in cure, is surgery (Fig. 4). All other therapies are either adjuvant or palliative. The surgical standard of primary colon carcinoma includes the radical resection of the tumor-bearing colon and the complete dissection of its lymphatic drainage area by central ligation of its vessels. The lymphatic dissection and the blood supply of the bowel determines the extent of colonic resection and must be performed as an en-bloc lymphadenectomy in order to provide good oncological results. Any neighbouring organ or structure involved by the tumor, e.g. small bowel, kidney, uterus or bladder, should also be resected en bloc with the primary tumor.

To further reduce the risk of intraoperative dissemination of tumor cells, the no-touch isolation technique calls for central ligation of the vessels and closure of the bowel lumen prior to the mobilization of the colon. The surgeon and the expertise of the hospital have repeatedly been identified as one of the most important prognostic factors for patients with colorectal carcinoma. Depending on the yearly case load, the training and the special interest of the surgeon in colorectal surgery, disease-specific survival varies significantly among surgeons. Therefore, colon cancer surgery should preferably be performed in specialized colon cancer centers applying the outlined surgical standards in the treatment of primary colon carcinoma, involvement of regional lymphatic nodes, involvement of neighboring organs, as well as existence or absence of distant metastases.

Moreover, the functional evaluation of the general health and organ function of the patient by experienced medical staff is inevitable to weight the possible risks and benefits of the treatment options (Fig. 3).

Fig. 4: High-tech operation theatres provide the best technology and lead to best surgical results.

Рис. 4: Высокотехнологичные операционные обеспечивают применение самых современных технологий и наилучшие хирургические результаты.

Хирургия
Основным методом терапии колоректального рака и единственным вариантом лечения, который может привести к выздоровлению, является операция (рис. 4).

Все остальные методы лечения являются адъювантными или паллиативными. Хирургический стандарт первичного колоректального рака включает в себя радикальную резекцию сегмента кишки с опухолью и полную диссекцию ее лимфодренажной системы путем центральной перевязки сосудов. Диссекция лимфатической системы и кровоснабжение кишки определяют степень резекции, которая должна быть выполнена единым блоком, чтобы обеспечить хороший онкологический результат.

Любой соседний пораженный опухолью орган или структура, например, тонкий кишечник, почки, матка или мочевой пузырь, также должны быть резецированы единым блоком с первичной опухолью. Чтобы еще больше снизить риск интраоперационного распространения опухолевых клеток, необходимо применять технику неприкосновенности (изоляцию пораженного органа до манипуляций на нем), что требует центральной перевязки сосудов и закрытия просвета кишки до ее мобилизации.

Квалификация и опыт хирурга и уровень больницы неоднократно назывались одними из важнейших прогностических факторов у пациентов с колоректальным раком. В зависимости от количества
Fig. 5: Removal of the right colon = right hemicolectomy
Рис 5: Удаление правой части толстой кишки – правосторонняя гемиколэктомия

Fig. 6: Removal of the left colon = left hemicolectomy
Рис 6: Удаление левой части толстой кишки – левосторонняя гемиколэктомия

Fig. 7: Removal of the sigmoid colon = sigmoid resection
Рис 7: Удаление сигмовидной кишки – сигмовидная резекция

Fig. 8: Removal of the rectum with preservation of continence = anterior resection
Рис 8: Удаление прямой кишки с сохранением сфинктера – передняя резекция
Fig. 9: Different techniques of pouch reservoirs after removal of the rectum with the aim to achieve a good continence. a. transverse coloplasty, b. side-to-end anastomosis, c. colonic J-pouch

Fig. 9: Различные техники формирования «мешка» -резервуара для кала после удаления прямой кишки для достижения хорошего регулирования стула: a – колопластика поперечной кишки; b – анастомоз «бок в конец»; c – кишечная J-сумка

Colon Cancer Therapy

Surgical Standards
Carcinoma of the coecum and ascending colon is treated with right hemicolectomy with central ligation of the iliac and right colonic arteries and reconstruction by ileo-transversostomy (Fig. 5). Carcinoma in the middle of the transverse colon is treated with transverse colectomy or extended right or left colectomy with truncal ligation of the middle, right and / or left colonic artery and reconstruction by ascendo-descendostomy. Carcinoma of the descending colon is treated with left hemicolectomy with central ligation of the inferior mesenteric artery and reconstruction by transverse-rectostomy (Fig. 6). Carcinoma of the sigmoid colon is treated with radical sigmoid resection with central ligation of the inferior mesenteric artery and reconstruction by descendo-rectostomy (Fig. 7). Colon carcinomas located in between two lymphatic drainage areas like carcinomas of the lateral transverse colon or the right (hepatic) and left (splenic) flexure are treated by extended right or left colectomies or subtotal colectomies with central ligation of the vessels of the two lymphatic drainage

Выполняемых операций в год, степени подготовки и особого интереса хирурга к колоректальной хирургии показатель выживаемости пациентов значительно варьирует у разных хирургов. Таким образом, хирургию колонэктомии желательно проводить в специализированных центрах, где следуют современным хирургическим стандартам лечения первичного колоректального рака, что обеспечивает наилучшие кратко- и долгосрочные результаты.

Хирургические методики
При раке слепой и восходящей ободочной кишки проводят правостороннюю гемиколэктомию с центральной перевязкой подвздошно-ободочной и правой толстокишечной артерии и формированием подвздошно-ободочного анастомоза (рис. 5). Рак средних сегментов поперечно-ободочной кишки лечится путем полной колэктомии или расширенной право- или левосторонней колэктомии с переводом стволов средней, правой и/или левой толстокишечных артерий и наложением восходяще-нисходящего анастомоза.

Рак нисходящей толстой кишки лечится посредством левосторонней гемиколэктомия с перевязкой нижней брыжеечной артерии и формированием поперечно-поясничного анастомоза (рис. 6)
areas. In rectal cancer surgery, we differentiate depending on the tumor location between sphincter-preserving (Fig. 8) and non sphincter-preserving procedures. Special techniques are developed as stool reservoirs after resection of the rectum and to ensure a good quality of continence and life (Fig. 9). Non-sphincter preserving techniques are performed rarely at our institution (Fig. 10). Our university hospital has a specialized team of internationally recognized surgeons and gastroenterologists, which work continuously on improvements in surgical techniques for colon and rectal cancer.

Laparoscopic Resection
Laparoscopic surgery for colon cancer is a recognized alternative to established open (conventional) surgery. Several studies have shown no disadvantages in regard to the extent of resection, number of resected lymph nodes and short- and long-term outcome (prognosis). However, it has to be realized that these study patients were often highly selected, and only highly experienced surgeons participated in the trials. We believe, that laparoscopic surgery should be considered primarily for colon cancer patients with small tumors and should be performed only by laparoscopic-trained surgeons, which can provide the same oncological quality as in conventional surgery. We developed several surgical techniques, which are performed by our minimal-invasive specialists at our university hospital (Fig. 11).

Adjuvant Therapy
The stage of disease at presentation remains the most important prognostic factor for colon cancer patients (Fig. 12). Stage I disease carries an excellent prognosis of more than 95% 5-year survival rate, and surgical treatment alone is considered sufficient. An adjuvant therapy is not indicated. Chemotherapy in an adjuvant setting is not justified.

Laparoscopic Resection
В хирургии рака прямой кишки, в зависимости от локализации, выполняются операции с сохранением сфинктера (рис. 8) и без его сохранения. Разработаны специальные методы по формированию резервуара кала после резекции прямой кишки для обеспечения регуляции стула и хорошего качества жизни (рис. 9). Методы без сохранения сфинктера в нашем институте применяются редко (рис. 10).

Наша университетская клиника имеет специализированную группу международно признанных хирургов и гастроэнтерологов, которые постоянно работают над улучшением хирургических методов лечения колоректального рака.

Лапароскопические операции
Лапароскопическая хирургия колоректального рака является признанной альтернативой открытой (обычной) операции. Несколько исследований не показали недостатков в отношении степени резекции, количества удаленных лимфатических узлов и кратко- и долгосрочных результатов (прогноза). Тем не менее нужно понимать, что в этих исследованиях участвовали специально отобранные пациенты и только опытные хирурги. Мы считаем, что лапароскопические методы показаны, прежде всего, для пациентов с небольшими опухолью и должны быть выполнены только специально подготовленными хирургами, что позволит обеспечить то же качество, что и обычная хирургия. Мы разработали несколько хирурги-
setting is recommended for patients with colon carcinoma without distant metastases after complete resection of the primary tumor and the lymphatic drainage area but elevated risk for tumor recurrence. These recommendations are based on the risk-benefit analysis according to the UICC/AJCC staging classification.

Adjuvant chemotherapy is recommended in stage III colon cancer (no distant metastases but resected local lymph node metastases) as it has proved to reduce the rate of tumour recurrence, to increase disease-free and overall survival and to be cost-effective in this patient group. For colon cancer stage II, adjuvant chemotherapy is currently not routinely recommended as the available randomized controlled trials have failed to demonstrate convincing survival benefits for the entire patient group. Nevertheless, high-risk situations are identified, in which adjuvant chemotherapy should be offered even to patients with UICC stage II disease.

Conclusion
Surgery is the only option for cure in the treatment of colon cancer (Fig. 13). The surgical standard in the treatment of primary cancer of the colon includes the radical resection of the tumor-bearing colon.

Colon Cancer Therapy
Colon Cancer Therapy

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with en-bloc lymphadenectomy and central ligation of its vessels. Open (conventional) or laparoscopic techniques can be applied to achieve good oncological results in colon cancer surgery. Adjuvant treatment has repeatedly been shown to improve survival in stage III (node-positive) disease. The role of adjuvant treatment for stage II (node-negative) disease remains controversial.

Literature


Fig. 13: Colorectal trained surgeon at the Department of Surgery, Klinikum rechts der Isar, Technische Universität Munich

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Dr. Ralf Gertler (MD)
Dr. Matthias Maak (MD)
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Let’s design the future
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 Epoque 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 splendidorous 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 many SPA-hotels, especially the ones in the Black Forest.

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 в двух термальных купальниках – современной Caracalla Spa (Спа Каракаллы) и исторической римско-ирландской Friedrichsbad (Фридрихсбад). Кроме того, многие SPA-отели, особенно комфортные для проживания и релаксации, 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 времяпровождением.

На протяжении более 350 лет три километра превосходнейшего парка и сада Lichtentaler Allee (Аллея Лихтенталера) являются зеленой и цветущей визитной карточкой Баден-Бадена. Соз-
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, bistro 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.

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(Фестшпильхаус), 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 Замка Неуэйера, выступления зарубежных артистов и исполнителей в «Фестшпильхаусе».

На живописных улицах и в переулках в стиле «нео-барокко» старого города Баден-Баден расположены многочисленные бутаны, которые приглашают на первоклассный 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.
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Department of Orthopaedic Sports Medicine, Klinikum rechts der Isar
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