AdvISAbILIty Of PALLIAtIvE RESEctIONS IN INcuRAbLE ADVANCED GAStRIc cANcER

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Effective treatment is the primary objective of surgeon in the treatment of advanced gastric cancer. Poor prognosis and significant advancement of gastric cancer at the time of diagnosis are decisive factors for the only possible surgical management method being palliative procedures.

The aim of the study was the evaluation of the value of palliative resection procedures in patients with advanced gastric cancer.

Material and methods. The subject in the study was a group of 105 patients with gastric adenocarcinoma at stage 4 of advancement, in whom curative treatment was not possible. The group constituted 44.5% of patients operated on due to gastric cancer at the Department of General and Oncological Surgery, PUM, in the years 1998-2009. The patients were divided into two groups: the first one comprised 44 patients post palliative resections, the second – 61 patients post non-resection procedures. The subject of analysis were early and late treatment results post palliative resections, and they were compared with the treatment results post non-resection procedures.

Results. Palliative resections were performed in 44 patients (19 females and 25 males), while in 61 patients (38 males and 23 females) non-resection procedures were performed. Postoperative complications were observed in 25% of patients in the group post palliative resections and in 11.5% in the group of patients without the resection of primary focus. In-hospital mortality stood at 4.5% in the group post palliative resections and 4.8% in the group post non-resection procedures. The percentage of 1-year and 4-year survival post palliative resections stood at 43% and 8.8%, respectively. In the group without the resection of primary focus, 16% survived 1 year and nobody survived 2 years.

Conclusions. Palliative resections improve the survival of patients with incurable gastric cancer and should be considered if only the loco-regional conditions are favourable.

Key words: gastric cancer, palliative resections, non-resection procedures

Gastric cancer is one of the most common cancers in humans. It leads both in incidence and in mortality due to neoplasms, despite the significant drop in gastric cancer incidence in all regions and on all continents, particularly in countries of the Western hemisphere (1). It is estimated that in 2008 there were diagnosed 988,600 new cases and 737,000 deaths were pronounced, and thus gastric cancer ranks fourth in terms of prevalence in males and fifth in females, as well as ranks third and fifth, respectively, among the most common causes of death due to cancer (2). In the same year, in Poland, there were diagnosed 5,100 new cases of the disease and 5,573 deaths pronounced (3). Effective treatment is the primary objective of gastric cancer surgery. The decisive factor in such treatment results is the disease advancement. Poor prognosis in gastric cancer is associated with the fact that in the majority of patients the disease is diagnosed at its advanced stage.

In Western countries, early gastric cancer is diagnosed only in 15-20% of patients, while in
Japan it is diagnosed in approx. 50% of patients, which explains the big differences in long-term treatment results between Japan and the rest of the world. For the same reason, curative treatment is possible only in 50-60% of patients, while in the remaining ones the only possible surgical management method are palliative procedures. This is why even patients post curative resections often die due to the disease recurrence (only 20-25% of patients with gastric cancer have a chance to survive 5 years) (4).

The main objective of palliative treatment is the improvement of the comfort of life or elimination of symptoms associated with the neoplastic disease, which eliminates the potential complications caused by the neoplastic tumour, such as haemorrhage, obstruction and pain. A disputable objective of palliative treatment is the prolongation of patient’s life.

The efficacy of palliative gastric resection due to cancer remains the subject of discussion and raises many controversies, and the data concerning such procedures are limited to retrospective analyses concerning heterogeneous patient groups. The majority of such analyses have indicated the beneficial effect of resection procedures on long-term results in advanced gastric cancer (5-8).

The aim of this study was the evaluation of the value of palliative resection procedures in the treatment of advanced gastric cancer, and the comparison of the results of palliative resections and non-resection procedures.

MATERIAL AND METHODS

In the period between 1 January 1998 and 30 November 2009, at the Department of General and Oncological Surgery, Pomeranian Medical University in Szczecin, there were hospitalized 261 patients with diagnosed gastric adenocarcinoma. 236 (90.4%) of them were qualified for surgery. In 175 (74.2% of those operated on) resection procedures were performed. The subject of this study was a group of 105 patients (44.5% of those operated on during that period) with advanced gastric cancer, in whom curative treatment was not possible due to the loco-regional advancement or distant organ metastases. The patients were divided into two groups; the first one (PR group) encompassed 44 patients post palliative resections, while the second (NP group) included 61 patients who had been treated surgically without the resection of primary focus. The group characteristics are presented in tab. 1.

The resection was deemed palliative if distant metastases were found or if the loco-regional advancement precluded the performance of R0 resection.

Analysed were the early results of surgical treatment, including postoperative complications and in-hospital mortality. In-hospital mortality was defined as death within 30 days post surgery. In addition, analysed were long-term treatment results and compared were the long-term survival between the group of patients post palliative resections (PR group) and the group of patients post surgeries without the resection of primary focus (NP group). The survival analysis was performed with the use of Kaplan-Meier curve, and the differences in survival were compared with the use of long-rank test.

RESULTS

Resection was deemed palliative in 44 patients (19 females and 25 males), which constituted 18.6% of all operated on and 25.1% of all resections due to gastric cancer in the analysed period. The criteria of classifying the procedure as palliative were based on the evaluation of advancement during the surgery. In the studied group, there were performed 9 sub-total and 35 total gastric resections. In the NP group, there were 61 patients operated on (38 males and 23 females); in 44 exploratory laparotomies were performed, 13 of patients required the gastric bypass surgery, while in

<table>
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<th>Table 1. Characteristics of the studied group</th>
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<td>PR group</td>
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<td>NP group</td>
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4 patients with gastric cardia cancer there were created feeding stomies (3 jejunostomies and 1 gastrostomy).

The studied groups did not differ significantly in terms of age or gender. The mean age of patients in whom palliative resections were performed was 61.4 (from 22 to 78), the mean age in the group of patients post non-resection surgeries was 61.9 (from 36 to 80).

The mean hospitalization period in the group post palliative resections was 16.9 days (from 8 to 124 days) and the median hospitalization period was 13 days, while in the NP group the mean hospitalization period was 13 days (from 6 to 33 days), and the median hospitalization period was 12 days.

In the resection group, the tumour was most commonly located in the 1/3 distal part of the stomach (in 19, i.e. 43% of those operated on), in the median part there were 13 tumours (in 29.5% of those operated on), in the 1/3 proximal part there were located 11 tumours (in 25% of those operated on). In the discussed group, the most commonly diagnosed type of cancer as per Lauren was diffuse adenocarcinoma, diagnosed in 22 patients (50% of those operated on). Intestinal carcinoma was diagnosed in 14 patients (32% of those operated on), while 8 patients were diagnosed with mixed-type carcinoma.

The main causes precluding the performance of radical surgery in the PR group were in order: peritoneal dissemination in 20 patients (45.4% of those operated on), liver metastases in 16 patients (36.4%), nodular dissemination precluding the performance of radical surgery was found in 10 patients (22.7%), in 3 patients (6.8%) ovarian metastases were found. In 5 patients from the discussed group there were found distant metastases to at least two organs.

Postoperative complications were seen in more often in the group post palliative resections. They were observed in 11 patients (25%) in the group post palliative resections and in 7 patients (11.5%) in the group of patients without the resection of primary focus (tab. 2).

Two patients post palliative resections required emergency relaparatomy due to complications, in one case leaking oesophagoenterostomy was seen, and in the second case the patient developed symptoms of diffuse peritonitis caused by the stoma in the duodenal stump. No complications requiring repeat surgery were observed in the NP group.

No significant difference in in-hospital mortality was observed between the studied groups. In the postoperative period there were observed 2 deaths in the PR group (in-hospital mortality: 4.5%) and 3 deaths in the NP group (mortality: 4.8%).

The comparison of survival in both studied groups revealed that the resection of primary focus had a significant impact on patient survival ($p=0.001$). The mean survival in the group post palliative resections was 10.5 month (median: 8.5 months). The mean survival post non-resection surgeries was 5.5 months (median: 6 months), hence the survival was almost twice longer in the group of palliative resections. The percentage of 1-year and 4-year survival post palliative resections was 43% and 8.8%, respectively. In the group without the resection of primary focus, 16% of patients survived 1 year, while nobody survived 2 years (fig. 1).

The presence of distant metastases correlated significantly with shorter survival in patients post palliative resections (fig. 2). Longer survival was also observed in patients with the tumour localized in the 1/3 distal part of the stomach (mean survival was 11.2 months as compared with 8.5 months in cancer localized in the more proximal parts of the stomach) and in the intestinal carcinoma (mean survival was 14 months as compared with 9.5 months in the disseminated type), but the differences in survival were not statistically significant. Other factors, such as age, gender, T and N advancement stage, did not have any impact on patient survival.

DISCUSSION

Despite the drop in gastric cancer incidence observed in recent decades, mortality due to it

<table>
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<tr>
<th>Complication type</th>
<th>PR group</th>
<th>NP group</th>
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<tr>
<td>Cardiorespiratory failure</td>
<td>3</td>
<td>2</td>
</tr>
<tr>
<td>Pneumonia</td>
<td>2</td>
<td>1</td>
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<tr>
<td>Lung oedema</td>
<td>2</td>
<td>2</td>
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<tr>
<td>Wound infection</td>
<td>2</td>
<td>2</td>
</tr>
<tr>
<td>Leaking oesophagoenterostomy</td>
<td>1</td>
<td>not applicable</td>
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<tr>
<td>Stoma in the duodenal stump</td>
<td>1</td>
<td>not applicable</td>
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Table 2. Postoperative complications in the studied groups
still leads (1). Only half of patients with gastric cancer have a chance of undergoing curative procedure, and still the majority of them will die due to the disease. The treatment results in gastric cancer are unsatisfactory, and the main reason is the disease diagnosis at its advanced stage (4, 9). The majority of studies on gastric cancer are limited to the evaluation of the results in a group of patients in whom it was possible to perform the curative procedure, while there are few studies analysing the fate of patients post palliative surgeries, and thus we decided to look into this problem. We decided to analyse the group of patients in whom gastric resections could not be deemed curative and to compare the results of surgical treatment with those of the group in which the resection procedure had not been performed. Efficacy of palliative gastric resection due to cancer remain the subject of discussion and raises many controversies, while the data concerning such procedures are limited to few retrospective analyses concerning heterogeneous patient groups (5-8, 10, 11). The majority of publications analysing the value of palliative resections in the treatment of advanced gastric cancer have similar methodological defects, stemming mainly from the lack of possibility of comparing objectively the groups of patients post palliative resections and post non-resection procedures. Since there had to exist some favourable conditions which had been crucial in making the decision on performing the resection procedure in some of them and not performing such procedure in others.

Furthermore, a large percentage of patients had not qualified at all for resection procedures due to local advancement of the disease. On the other hand, the lack of possibility of performing randomized prospective studies does not leave any other choice.

Table 3 present the comparison of results post palliative resection procedures in advanced gastric cancer published by different authors. The results of our analyses demon-

<table>
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<th>Author</th>
<th>No of patients</th>
<th>In-hospital mortality (%)</th>
<th>Hospitalization period (in days)</th>
<th>Incidence of postoperative complications</th>
<th>Mean survival (in months)</th>
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<tr>
<td>Hartgrink et al.</td>
<td>156</td>
<td>12.00%</td>
<td>15</td>
<td>38%</td>
<td>14.3</td>
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<td>Huang et al.</td>
<td>365</td>
<td>3.30</td>
<td>15</td>
<td>20%</td>
<td>10.2</td>
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<td>Saidi et al.</td>
<td>24</td>
<td>8.7</td>
<td>15</td>
<td>33.3</td>
<td>16.3</td>
</tr>
<tr>
<td>Miner Thomas et al.</td>
<td>307</td>
<td>6</td>
<td>16.9</td>
<td>54</td>
<td>10.6</td>
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<tr>
<td>Doglietto et al.</td>
<td>93</td>
<td>11.8</td>
<td>-</td>
<td>33.3</td>
<td>16.3</td>
</tr>
<tr>
<td>Authors</td>
<td>44</td>
<td>4.50</td>
<td>16.9</td>
<td>25%</td>
<td>10.5</td>
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strated a beneficial impact of palliative resections on long-term survival of patients with advanced gastric cancer, with low risk of periprosthetic mortality and acceptable risk of perioperative complications. Despite the fact that the benefits stemming from palliative resections in advanced gastric cancer are disputable according to many authors (7, 8, 11, 12), our analyses confirm the beneficial impact of such procedures, similarly to the majority of reported retrospective studies analysis the value of such resections (10, 13, 14, 15).

Some studies have suggested that palliative resections are associated with high risk of perioperative complications and high mortality. In the study conducted by Hartgrink and colleagues, postoperative complications have been observed in 38% of patients in whom palliative resections had been performed, and the mortality rate has reached 12% (12). In our analyses, no significant differences in in-hospital mortality were observed between the group post palliative resections and post non-resection procedures, and the risk of in-hospital death in both groups was < 5%. Similar results have been obtained in the study conducted by Huang and colleagues, in which the in-hospital mortality have stood at 3.3% and has not differed significantly from mortality in the non-resection group (15). We found significantly higher incidence of complications in the group of patients post palliative resections (25% vs 11.5%), but the risk of complications was at an acceptable level. The percentage of postoperative complications was at a level similar to that in the abovementioned study by Huang and colleagues, and stood at approx. 20%.

We observed significantly longer hospitalization post palliative resections as compared with non-resection procedures (16.9 vs 13 days). Similar differences have been found in the study reported by Hartgrink and colleagues (15 vs. 10 days). The measure of beneficial impact of palliative resection procedures in our study was twice longer mean survival of patients as compared with non-resection procedures (10.5 vs 5.5 months). Similar differences have been observed in the study conducted in the Netherlands by the group studying gastric cancer (the Dutch Gastric Cancer Trial); the mean survival of patients post resection procedures as compared to non-resection procedures in the discussed study was 14.3 vs 8 months (12). Similar study results have been published by Huang and colleagues. In that study, the mean survival of patients post resection procedures was also twice longer as compared with that post non-resection procedures (10.2/4.8 months) (15.). Even bigger differences have been observed in the study reported by Saidi and colleagues. The mean survival of patients post palliative resections in that study was almost three times longer than that post non-resection procedures (16.3 vs 5.9 months) (14).

CONCLUSIONS
1. Palliative resection should be considered in each case of advanced gastric cancer, if the conditions enable the performance of such a procedure.
2. Palliative resections have a beneficial impact on the improvement of long-term survival among patients with incurable advanced gastric cancer.
3. Palliative resections are safe procedures since the risk of perioperative death is relatively low and comparable to the risk of death post non-resection procedures in incurable gastric cancer.
4. The only factor significantly affecting the survival of patients post palliative resections is the presence of distant metastases.

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COMMENTARY

The first decade of the 21st century confirms the downward trend in the incidence of gastric cancer worldwide. This trend is also reflected in epidemiological data from our country. However, invariably, the prognosis and long-term treatment results in gastric cancer, with the exception of Far Eastern countries, remain at an unsatisfactory level in the majority of countries of the so-called Western World. Multi-centre studies conducted in Poland since the 1980s by the Scientific Research Committee and the Ministry of Scientific Research and Information Technology, coordinated by Prof. Tadeusz Popiela, and recently by Prof. Jan Kulig, the executors of which have been, among others, the authors of the publication commented on and the author of comments, created an opportunity of improving the treatment results in gastric cancer to the level comparable with Western European countries and the USA.

Poland may take pride in having one of the largest well-documented databases of patients treated for gastric cancer in the world. The unique Polish material has been the subject of many publications in renowned medical journals, and “the Polish model” of combined treatment of gastric cancer has been quoted on many occasions as model one.

Unfortunately, when analysing Polish data from recent years there is evident an unfavourable upward trend in the numbers of advanced gastric cancer cases, which clearly translates into the deterioration in the results of 5-year survival of patients treated for cancer. The reasons for such trends are sought in, among others, a too-late diagnosis of cancer at the stage of both the initial qualification for gastric cancer diagnostics made by general practitioners at the onset of first disease symptoms and during the prolonged period between diagnosis and making the therapeutic decisions.

It is also unfortunate to state that the standard of care in combined treatment of gastric cancer outside the centres taking part in studies coordinated by the Krakow Centre is relatively rarely executed. Despite the principles of gastric cancer diagnostics and treatment binding in Poland, published, among others, as the so-called Polish consensus in “Polski Przegląd Chirurgiczny”, as well as the constantly updated gastric cancer treatment guidelines available in the materials of the European Society for Medical Oncology, International Gastric Cancer Association, NCCN Clinical Practice Guidelines in Oncology - National Comprehensive Cancer Network, the manner of treating gastric cancer in Poland leaves a lot to be desired. There are no precise epidemiological data concerning the numbers of recorded new cases of gastric cancer, the treatment method, stan-
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...dard of combined treatment, quality in terms of radicalness and oncological completeness of surgical treatment, as well as precise monitoring of long-term results.

Taking into account the worrying downward trend, low percentage of diagnosis of early advancement stages (the so-called early gastric cancer), determining the achievement of optimally beneficial treatment results, it is not surprising that the majority of cases encountered in Poland represent the disease stages with locally advanced gastric cancer or with disseminated neoplastic disease often determining the lack of possibility of radical treatment and thus the achievement of total and disease-free survival results comparable to those in Western countries.

The study commented on should be seen as commendable. Being aware of the unfavourable prognosis, the authors attempted palliative treatment in patients with advanced gastric cancer. Taking into account the currently binding guidelines, the fact of attempting by the paper authors the palliative gastric resection due to cancer might be disputable. From the purely humane point of view, each of us, surgeons, tries to perform resection in each case of gastric cancer. However, local, regional advancement or presence of metastases in gastric cancer make the surgeon face a difficult choice of exploratory laparotomy, performing bypasses, attempts of surgical or endoscopic patency restoration, implantation of prostheses for neoplastic stricture of the cardia, pylorus, the insertion of feeding stoma, or the performance of palliative gastric resection. According to the prevailing opinions, partial or total palliative gastric resection plays a role only in the improvement of comfort of life, and in fact has no significant impact on the prolongation of patient survival.

The essence of palliative gastric resection due to cancer is the maximal reduction of primary tumour mass without the possibility of oncologically radical procedure type R0, with assumed leaving locally the neoplastic tissue, or gastric cancer metastases impossible to be surgically removed.

Already in the monograph entitled “Rak żołądka” [Gastric cancer], ed. Prof. Tadeusz Popiela, in 1987 there was presented a position that in cases of inoperable gastric cancer the principle of palliative resection procedure applies, if the local conditions and the patient’s clinical condition allow this. A similar stand was presented by an expert group in the so-called Polish consensus on gastric cancer treatment in 2001, as well as in the joint work of TChP and PTChO of 2003.

However, the last decade is a completely new approach to practicing medicine, including also in the area of modern approach to making therapeutic decisions in gastric cancer. The principles of evidence-based medicine (EBM) implemented several years earlier have become the new and absolutely binding paradigm in modern medicine, including in gastric cancer treatment.

In 2001, The New York Times Magazine deemed EBM in its The Year in Ideas ranking the most influential idea of 2001, and the Editorial Board of the British Medical Journal classified the EBM principles as one of the 10 most important events to revolutionise medicine in the last 160 years and to become the basis of modern clinical practice and a completely different style of methodologically correct surgical practice. As a result of the above changes, the professional, as per EBM, and thus optimal, treatment of gastric cancer should be based on 3 principles: good knowledge of aetiology and the principles of gastric cancer pathophysiology, adequate own experience, with simultaneous use of experience of the so-called authorities in the given field, but above all on the analysis of information with treatment individualisation based on data having the highest level of record (meta-analyses of multicentre, prospective, randomised studies) with simultaneous the highest level of recommendations (full consensus of experts on the proposed diagnostic and therapeutic principles).

In view of the above, the currently binding practical guidelines of ESMO and NCCN, taking into account the EBM principles of 2010-2011, precisely define the indications in which the performance of palliative resection in gastric cancer in factually justified. The palliative gastric resection is recommended in cases of neoplastic disease complications such as haemorrhage, obstruction, perforation, pain.

According to the ESMO recommendations, each palliative gastric resection due to cancer is treated as an element of interdisciplinary therapeutic approach taking into account the biological differences of cancers and individual patient characteristics. In many cases, an...
alternative for palliative resection may be radiation therapy methods and to a lesser extent – chemotherapy.

According to the NCCN guidelines, palliative resection in gastric cancer should simply not be performed until the clinical symptoms of haemorrhage or obstruction, etc. appear. Meanwhile, this type of surgical palliative approach is acceptable, even with the confirmed positive margins (R1, R2), with the aim of alleviating the clinical manifestations of symptoms of neoplastic disease complications, or due to the emergency indications for saving the life of a patient with haemorrhaging, perforated or showing the symptoms of severe obstruction gastric cancer. After the gastric resection without the possibility of performing R0-type surgery, there are no indications either for the radicalness of lymph node resection.

Accepting fully the above recommendations, yet at the same time approaching them critically, similarly to the study authors I am a proponent of resecting advanced gastric cancer, even in patients with neoplastic dissemination to the peritoneal cavity, infiltration of important vascular structures, or the presence of metastases suggesting the inoperability of gastric cancer, since I can quote similarly many cases from own experience, as well as publications from both Polish multicentre studies and from international literature, which evidence the statistically significant differences in patient survival depending on the level of radicalness of R0-R1-R2 gastric cancer resection as independent prognostic factors.

Overall, along with making the decision on the performance of palliative gastric resection, there should be taken into account the indications for combined therapy, using both standard options of pre-operative and postoperative chemotherapy, radiation therapy or chemo- and radiation therapy. Unfortunately, this problem is not addressed by the study authors. Some hope in this regard may be associated with the monitoring of HER2 expression in cancer and with the so-called targeted therapy, with potential benefits for HER2 positive patients.

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