

# Metastases of gastric cancer into the liver – the authors' own experience and literature review

Marek Krawczyk, Michał Skalski, Michał Grąt, Piotr Krawczyk, Oskar Kornasiewicz

*Department of General, Transplant and Liver Surgery, Medical University of Warsaw, Poland*

**Introduction.** Synchronous metastases of gastric cancer to the liver occur in 3–14% of patients with this cancer, and metachronous lesions in 37% of patients after radical gastrectomy. Liver resections due to metastases of gastric carcinomas represent only 5–9% of resections due to metastases other than colorectal cancer. Until recently, patients with gastric carcinoma metastases to the liver were classified in the IV stage of cancer and the therapy was limited to chemotherapy or palliative treatment only.

**Material and methods.** The paper presents a current review of literature and the authors' own experience with liver resection due to gastric cancer metastases into this organ. During 34 months, 488 patients with liver metastases were treated in the Department of General, Transplant and Liver Surgery, of the Medical University of Warsaw, in whom 426 surgical procedures were performed (87.3%). The types of surgical procedures are as follows: minor liver resections in 204 patients (47.9%), hemihepatectomies in 102 patients (23.9%), thermoablations in 86 patients (20.2%) and laparotomies in 34 patients (8.0%). Among patients treated for liver metastases there were 4 patients with metastases from gastric cancer (0.8%), which constituted 1% of patients operated on, but 6.8% of patients with liver metastases from organs other than colorectal cancer. The postoperative course and direct results in all patients operated because of gastric cancer metastases into the liver were very good.

**Conclusions.** In some patients (single metachronous metastasis, no extrahepatic lesions, no peritoneal lesions, with subsequent chemotherapy) liver resection due to metastases from gastric cancer provides a chance for a longer survival.

NOWOTWORY J Oncol 2019; 69, 1: 1–6

**Key words:** gastric cancer, metastases, liver, surgical treatment

## Introduction

Synchronous metastases of gastric cancer to the liver occur in 3–14% of patients [1, 2], and metachronous lesions – in 37% of patients after radical gastrectomy [3]. These percentages are similar to the group of patients with colorectal cancer metastases to the liver. Liver resections due to metastases of gastric carcinomas, however, constitute only 5–9% of resections due to metastases other than colorectal cancer [4–7].

This is due, among other things, to the fact that until recently, patients with metastases of gastric cancer into the liver were disqualified from surgical treatment and offered chemotherapy only. Such an approach was based on the Japanese classifi-

cation of gastric cancer, indicating that patients in this period of cancer development belong to the IV stage of the disease, therefore the therapy should be limited to chemotherapy or palliative treatment [8].

One of the factors that influence the negative decision to remove metastases of gastric cancer from the liver is the coexistence of these metastases with metastases to other organs and structures – to the peritoneum or lymph nodes [6]. Moreover, single metastases of gastric cancer into the liver occur in only 0.5% of patients [9].

In 2008, a randomized Japanese and Korean study was published, which shed new light on the treatment of gastric

cancer patients with single stage factor, i.e. a liver metastasis [10]. Since then, the approach of surgeons has been changing and they more and more often remove gastric cancer metastases from the liver [11–14].

## Material

At the Department of General, Transplant and Liver Surgery of the Medical University of Warsaw, 488 people were treated within 34 months due to liver tumor metastases. In the whole group, patients with gastric cancer metastases constituted 0.8% (4 patients) (Tab. I). After analyzing the number of patients with liver metastases only from organs other than colorectal cancer, it turned out that the percentage of patients with metastases of gastric cancer was already 6.8% (Tab. II).

Out of all 488 patients with liver cancer metastases, 426 patients (87.3%) received surgery (Tab. III).

**Table I.** Patients with liver metastases

Primary lesion	Number of patients	Percentage
Colorectal cancer	429 patients	87.9%
Eye or skin melanoma	18 patients	3.7%
Kidney cancer	9 patients	1.8%
Ovarian cancer	9 patients	1.8%
Sarcoma (various primary locations)	8 patients	1.6%
GIST	6 patients	1.2%
Lung cancer	5 patients	1.0%
Gastric cancer	4 patients	0.8%
Total	488 patients	100%

**Table II.** Patients with liver metastases only from tumors other than colorectal cancer

Primary lesion	Number of patients	Percentage
Eye or skin melanoma	18 patients	30.5%
Kidney cancer	9 patients	15.2%
Ovarian cancer	9 patients	15.2%
Sarcoma (various primary locations)	8 patients	13.6%
GIST	6 patients	10.2%
Lung cancer	5 patients	8.5%
Gastric cancer	4 patients	6.8%
Total	59 patients	100%

**Table III.** Types of surgeries in patients with liver metastases

Surgery type	Number of patients	Percentage
Minor liver resection*	204 patients	47.9%
Hemihepatectomy	102 patients	23.9%
Thermoablation	86 patients	20.2%
Laparotomy	34 patients	8.0%
Total	426 patients	100%

\*According to the international classification – resection of < 2 liver segments

Four patients were operated on because of gastric cancer metastases. In three of them there were metachronous metastases, and in one – synchronous metastases. In one patient metachronous liver metastases occurred 27 years after gastrectomy. Polycyclic lesions were located at the border of segments II, III, IVA and IVB (Fig. 1). Metastatic lesions also appeared in the lymph nodes over the proper hepatic artery. A left hemihepatectomy was performed in this patient (Fig. 2–4) and lymph nodes from the proper hepatic artery area were excised. In the postoperative course a short-term bile leak was observed.

In the second patient, the metastasis to the VI segment of the liver (Fig. 5) has occurred 3 years after gastrectomy due to cancer. In this case, the resection of the VI segment of the liver was performed (Fig. 6) and the postoperative course was free from complications.

In turn, in the third patient two metachronous liver metastases (first to IV segment, and the second to VI segment) appeared one year after gastrectomy due to cancer. Liver segment VI was removed and left hemihepatectomy was performed. The postoperative course was also free of complications.

The fourth patient had a synchronous metastasis to the II and III segments of the liver. He underwent simultaneous gastrectomy and non-anatomic resection of the II/III segment of the liver. Postoperative treatment proceeded without complications.

Figures 1–4 show metastases of gastric cancer located on the border of segments II, III and IV of the liver.

If the tumor lesions are smaller and located more superficially, more limited liver resection can be performed with a sufficient oncological margin (Fig. 5–6).

The scope of liver resection depended on the location of the metastatic lesion (Tab. IV). Moreover, all four patients received adjuvant chemotherapy.

Two of the operated patients are still alive – one with metachronous metastasis (15 months after liver resection) and the other with synchronous metastasis (14 months after gastrectomy and liver resection). However, the patient with liver metastasis and lymph nodes over the liver artery died 3 months after the operation. The patient with a single metastasis to the VI segment of the liver also died – 9 months after the surgery.

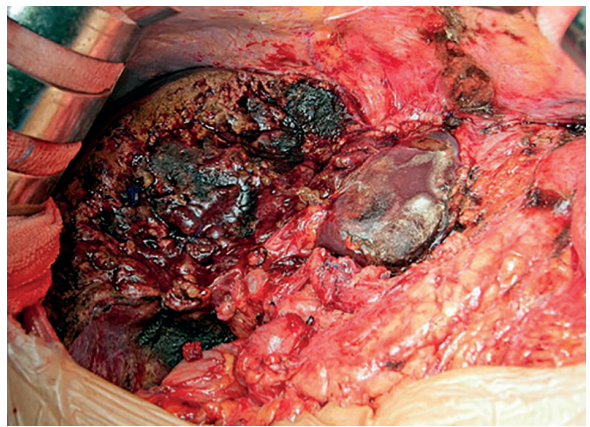
## Discussion

Gastric cancer, especially in China, Japan and Korea, is a common neoplasm. It is less common in European countries and the United States, but, which is particularly important, many patients are diagnosed with advanced cancer because there are no characteristic early symptoms and screening outside Japan is not carried out. Gastric cancer often causes metastases to many organs and structures at the same time: peritoneum, liver, lymph nodes. As result, only a few patients with metastatic lesions to the liver can undergo liver resection.

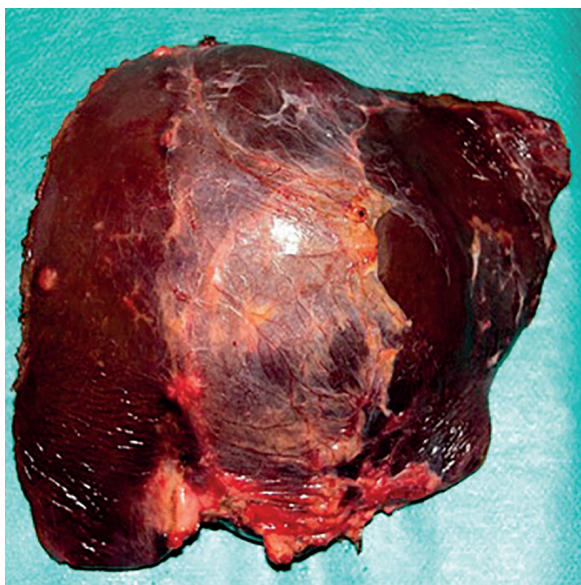
Not all prognostic factors for patients with metastases of gastric cancer into the liver (especially for patients with syn-



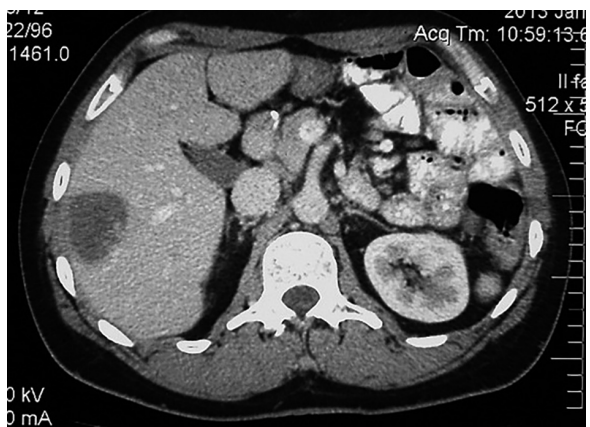
**Figure 1.** Computed tomography of a patient with a gastric cancer metastasis on the border of segments II, III and IV of the liver



**Figure 4.** Condition after left hemihepatectomy (the same patient as in Fig. 1)



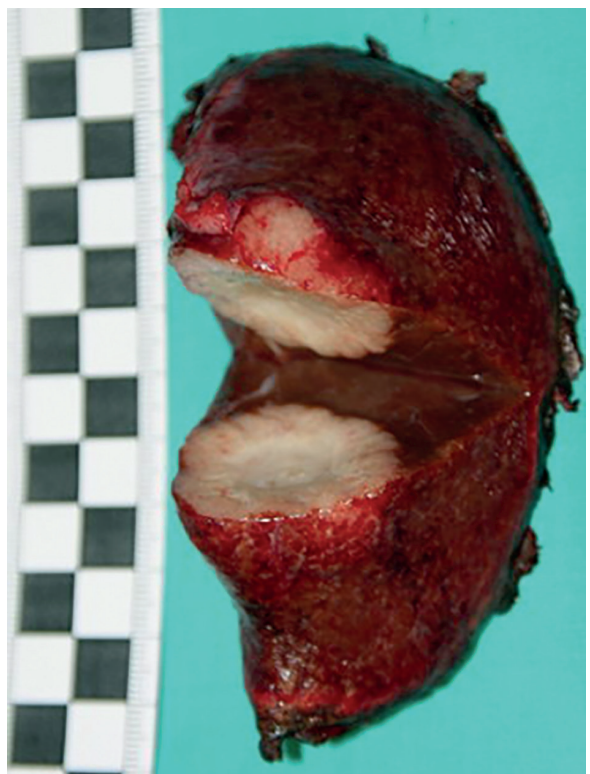
**Figure 2.** Preparation – left hemihepatectomy (the same patient as in Fig. 1)



**Figure 5.** Computed tomography of a patient with metastasis from gastric cancer to the VI liver segment



**Figure 3.** A cut-through preparation – left hemihepatectomy (the same patient as in Fig. 1)



**Figure 6.** Preparation after resection of a metastasis in segment VI of the liver

**Table IV.** Patient survival time after liver resection and follow-up time

Time to develop metastasis to the liver	Location of the metastatic lesion	Surgery type	Survival time after liver resection	Cause of death
Liver metastasis in 27 years after gastrectomy	On the border of segments II, III, IVA and IVB	Left hemihepatectomy and lymphadenectomy	3 months	Cancer relapse leading to stricture of bile ducts and biliary sepsis
Liver metastasis in 3 years after gastrectomy	Segment VI	Resection of segment VI	9 months	Extensive form of cancer disease – including bone metastases
Liver metastases in one year after gastrectomy	Segments IV and VI	Left hemihepatectomy and resection of segment VI	The patient lives – 15 months after liver resection	
Synchronous metastasis to the liver	Segments II and III	Simultaneous gastrectomy and excision of segments II and III of the liver	The patient lives – 14 months after simultaneous gastrectomy and liver resection	

chronous metastases) are known. It is known, however, that the prognosis for these patients is bad.

There are two types of prognostic factors: the first is related to the primary tumor and the second to the liver factor. The well-known factors, which are associated with the primary tumor and influence the survival of patients with gastric cancer, include: the depth of gastric wall infiltration by the tumor tissue and the coexistence of lymph node metastases [15, 16]. However, there are publications that question the importance of these prognostic factors in patients with hepatic metastases [17].

One of the important prognostic factors for survival of patients with metastases to the liver is the number of metastases. In the case of single lesions the 5-year survival rate is as much as 55% [15], while at numerous metastases it is 0% [18, 19]. In several studies, in case of single metastases, the tumor size was also taken into account as a prognostic factor [16], but this observation was not confirmed by other authors [20].

The 5-year survival of patients with single metastases of gastric and colorectal cancer was compared to that of the liver. The results were very similar [21]. However, 5-year survival after liver resection due to multi-site metastases of gastric cancer is much lower than in patients with colorectal cancer metastases [22, 23]. It was also analyzed whether synchronous metastases to the liver should be considered as a contraindication to the resection of this organ. In the authors' opinion, there are no grounds for this [22]. However, we should not overlook another publication the authors of which express the opposite opinion. It is justified by the findings that patients with synchronous metastases of gastric cancer to the liver also have extrahepatic metastases, and the disease itself is very advanced in the stomach [24].

The course of recurrent metastases of gastric cancer and colorectal cancer to the liver was also compared. It turned out that in the case of gastric cancer the recurrence of the disease occurred earlier than in colorectal cancer. In addition, the majority of patients with recurrent gastric cancer were not eligible for repeated surgery. On this basis, the oncological

aggressiveness of gastric cancer metastases was estimated to be much higher than colorectal cancer metastases [25].

An important issue is also performing repeated liver resections in case of recurrence of metastases to this organ. To this day, however, there is no clear answer as to whether repeated liver resection prolongs the lives of patients with gastric cancer [26].

In one publication it was pointed out that the presence of a fibrous pseudocapsule around the metastasis is a beneficial prognostic factor in metastases of gastric cancer into the liver. This should be explained by the fact that it occurs as a defensive reaction of an immunological and inflammatory nature against a metastatic lesion. This, in turn, would serve to stop further infiltration of the cancer process [26].

Chemotherapy is a separate issue in patients with metastases of gastric cancer into the liver. Chemotherapy – as the only form of treatment of patients with liver metastases – gives worse results than the surgical treatment combined with subsequent chemotherapy. Adjuvant chemotherapy is considered mandatory after metastatic resection [27].

Some publications stress that patients who cannot have liver resection with a metastatic lesion of gastric cancer should undergo a tumor thermoablation. Such action gives patients a chance for longer survival [28, 29].

In 2017, a summary of a review-based work [30] concluded that liver resection with gastric cancer metastases gives a longer median of patients' survival compared to palliative treatment. However, the authors stated that the final confirmation of such a position requires randomized studies.

A comprehensive summary of the knowledge on liver resection with metastases from gastric cancer is presented in several other publications from recent years [31, 32]. The authors emphasize that two types of prognostic factors should be taken into account: one concerns the primary tumor and the other the metastatic lesion in the liver. Factors related to the primary tumor include the stage of the tumor, which should not exceed the T2 stage of the tumor. On the other hand, the liver factor is connected with the number and size

of metastatic lesions. Patients with single metastases to the liver with a diameter of < 4 cm and metachronous metastases have the best prognosis.

A similar meta-analysis was presented in *Annals of Surgery* in 2016 [33]. It confirms that liver resection with single metastases of gastric cancer in patients without peritoneal spreading is a viable option: 1 year – in 68% patients, 2 years – in 31% and 5 years – in 27% patients. These results are more favorable than after treatment with cytostatic agents only, because in this group only 46% of patients experiences one-year survival. The same study emphasizes that the success of treatment depends on the oncological margin during liver resection, the severity of lesions in the lymph nodes and the presence of neoplastic lesions in venous blood vessels. In the majority of patients liver resections were of a minor nature (< 2 segments). The authors of this study also observed that in the Far East the results of resection treatment are better than in the West.

In another publication, a Korean group of surgeons evaluated the results of resection of metastases of gastric cancer into the liver in relation to the primary tumor. They showed that patients with type I or II according to pathomorphological classification of gastric cancer and intestinal form of gastric cancer have better prognosis [34]. Once again, it was pointed out that the results of liver resection are influenced by the type and degree of advancement of the primary tumor.

## Conclusions

Finally, other publications [35, 36] and results obtained by our clinic (although they concern a small group of patients, as in other single liver surgery centers) indicate that in some patients (single metachronous metastasis, no extrahepatic lesions, no peritoneal lesions, with subsequent chemotherapy) liver resection due to gastric cancer metastases offers a better chance of survival than just chemotherapy.

**Conflict of interest:** none declared

### Marek Krawczyk

Medical University of Warsaw

Department of General, Transplant and Liver Surgery

ul. Banacha 1a

02–097 Warszawa, Poland

e-mail: marek.krawczyk@wum.edu.pl

Received: 8 Jan 2019

Approved for printing: 13 Feb 2019

## References

1. Saiura A, Umekita N, Inoue S et al. Clinicopathological features and outcome of hepatic resection for liver metastasis from gastric cancer. *Hepatogastroenterology* 2002; 49: 1062–1065.
2. Zacherl J, Zacherl M, Scheuba C et al. Analysis of hepatic resection of metastasis originating from gastric adenocarcinoma. *J Gastrointest Surg* 2002; 6: 682–689.
3. D'Angelica M, Gonen M, Brennan MF et al. Patterns of initial recurrence in completely resected gastric adenocarcinoma. *Ann Surg* 2004; 240: 808–816.

4. Thelen A, Jonas S, Benckert C et al. Liver resection for metastatic gastric cancer. *Eur J Surg Oncol* 2008; 34: 1328–34.
5. Adam R, Chiche L, Aloia T et al. Hepatic resection for noncolorectal nonendocrine liver metastases. *Ann Surg* 2006; 244: 524–535.
6. Kornasiewicz O, Ligocka J, Krawczyk M. Liver resection for non-colorectal, non-endocrine liver metastasis. *Pol. J. Surg* 2014; 86: 544–551.
7. Gandy RC, Bergamin PA, Haghighi KS. Hepatic resection of non-colorectal non-endocrine liver metastases. *ANZ J Surg* 2017; 87: 810–814.
8. Japanese Gastric Cancer Association. Japanese classification of gastric carcinoma: 3rd English edition. *Gastric Cancer* 2011; 14: 101–12.
9. Linhares E, Monteiro M, Kesley R et al. Major hepatectomy for isolated metastases from gastric adenocarcinoma. *HPB (Oxford)* 2003; 5: 235–237.
10. Fujitani K, Yang H, Kurokawa Y et al. Randomized controlled trial comparing gastrectomy plus chemotherapy with chemotherapy alone in advanced gastric cancer with a single non-curable factor. Japan Clinical Oncology Group Study JCOG0705 and Korea Gastric Cancer Association Study KGCAO. *Jpn J Clin Oncol* 2008; 38: 504–506.
11. Miki Y, Fujitani K, Hirao M et al. Significance of surgical treatment of liver metastases from gastric cancer. *Anticancer Research* 2012; 32: 665–670.
12. Kerkar SP, Kemp CD, Avital I. Liver resections in metastatic gastric cancer. *HPB (Oxford)* 2010; 12: 589–596.
13. Fitzgerald TL, Brinkley J, Banks S et al. The benefits of liver resection for non-colorectal, non-euroendocrine liver metastases: a systematic review. *Langenbecks Arch Surg* 2014; 399: 989–1000.
14. Garancini M, Uggeri F, Degrate L et al. Surgical treatment of liver metastases of gastric cancer: is local treatment in a systemic disease worthwhile? *HPB* 2012; 14: 209–215.
15. Koga R, Yamamoto J, Ohyama S et al. Liver resection for metastatic gastric cancer: experience with 42 patients including eight long-term survivors. *Jpn J Clin Oncol* 2007; 37: 836–42.
16. Kumagai K, Tanaka T, Yamagata K et al. Liver metastasis in gastric cancer with particular reference to lymphatic advancement. *Gastric Cancer* 2001; 4: 150–5.
17. Sakamoto Y, Sano T, Shimada K et al. Favorable indications for hepatectomy in patients with liver metastasis from gastric cancer. *J Surg Oncol* 2007; 95: 534–9.
18. Cheon SH, Rha SY, Jeung HC et al. Survival benefit of combined curative resection of the stomach (D2 resection) and liver in gastric cancer patients with liver metastases. *Ann Oncol* 2008; 19: 1146–53.
19. Garancini M, Uggeri F, Degrate L et al. Surgical treatment of liver metastases of gastric cancer: is local treatment in a systemic disease worthwhile? *HPB (Oxford)* 2012; 14: 209–15.
20. Tsujimoto H, Ichikura T, Ono S et al. Outcomes for patients following hepatic resection of metastatic tumors from gastric cancer. *Hepatology* 2010; 4: 406–13.
21. Cummings LC, Payes JD, Cooper GS. Survival after hepatic resection in metastatic colorectal cancer: a population-based study. *Cancer* 2007; 109: 718–26.
22. Kornprat P, Jarnagin WR, Gonen M et al. Outcome after hepatectomy for multiple (four or more) colorectal metastases in the era of effective chemotherapy. *Ann Surg Oncol* 2007; 14: 1151–60.
23. Qiu J-L, Deng M-G, Li W et al. Hepatic resection for synchronous hepatic metastasis from gastric cancer. *EJSO* 2013; 39: 694e700.
24. Ueda K, Iwahashi M, Nakamori M et al. Analysis of the prognostic factors and evaluation of surgical treatment for synchronous liver metastases from gastric cancer. *Langenbecks Arch Surg* 2009; 394: 647–653.
25. Oguro S, Imamura H, Yoshimoto J et al. Liver metastases from gastric cancer represent systemic disease in comparison with those from colorectal cancer. *J Hepatobiliary Pancreat Sci* 2016; 23: 324–332.
26. Okano K, Maeba T, Ishimura K et al. Hepatic resection for metastatic tumours from gastric cancer. *Ann Surg* 2002; 235: 86–91.
27. Koizumi W, Narahara H, Hara T et al. S-1 plus cisplatin versus S-1 alone for first-line treatment of advanced gastric cancer (SPIRITS trial): a phase III trial. *Lancet Oncol* 2008; 9: 215–21.
28. Kim HO, Hwang SI, Hong HP et al. Radiofrequency ablation for meta-chronous hepatic metastases from gastric cancer. *Surg Laparosc Endosc Percutan Tech* 2009; 19: 208–12.
29. Chen J, Tang Z, Dong X et al. Radiofrequency ablation for liver metastasis from gastric cancer. *EJSO* 2013; 39: 701e706.
30. Liao Y-Y, Peng N-Fu, Long D et al. Hepatectomy for liver metastases from gastric cancer: a systematic review. *BMC Surgery* 2017; 17: 14, 1–7.
31. Tiberio GAM, Roviello F, Donini A et al. The Italian Research Group for Gastric Cancer. Hepatic metastases from gastric cancer: A surgical perspective. *World J Gastroenterol* 2015; 21: 11489–11492.

32. Baek H-U, Kim SB, Cho E-H et al. Hepatic Resection for Hepatic Metastases from Gastric Adenocarcinoma. *J Gastric Cancer* 2013; 13: 86–92.
33. Markar SR, Sameh Mikhail S, Malietzis G et al. Influence of Surgical Resection of Hepatic Metastases From Gastric Adenocarcinoma on Long-term Survival: Systematic Review and Pooled Analysis. *Ann Surg* 2016; 263: 1092–1101.
34. Shin S-H, Kim JM, Kim SM et al. Metachronous liver metastasis after curative gastrectomy for gastric adenocarcinoma. *Korean J Clin Oncol* 2014; 10: 84–91.
35. Martella L, Bertozzi S, Londero AP et al. Surgery for Liver Metastases From Gastric Cancer. A Meta-Analysis of Observational Studies. *Medicine* 2015; 94: 1–9.
36. Tiberio GAM, Roviello F, Donini A et al. On behalf of the Italian Research Group for Gastric Cancer. Surgery for liver metastasis from gastric cancer. *Transl Gastroenterol Hepatol* 2016; 1: 68, 1–3.