

Advanced age remains an achilles heel for liver resections.

Laurent Sulpice, Michel Rayar, Boris Campillo, Claire Pery, Antoine Guillaud, Bernard Meunier, Karim Boudjema

► **To cite this version:**

Laurent Sulpice, Michel Rayar, Boris Campillo, Claire Pery, Antoine Guillaud, et al.. Advanced age remains an achilles heel for liver resections.. World Journal of Surgery, Springer Verlag, 2014, 38 (4), pp.918-26. 10.1007/s00268-013-2367-0 . hal-00990299

HAL Id: hal-00990299

<https://hal-univ-rennes1.archives-ouvertes.fr/hal-00990299>

Submitted on 13 May 2014

HAL is a multi-disciplinary open access archive for the deposit and dissemination of scientific research documents, whether they are published or not. The documents may come from teaching and research institutions in France or abroad, or from public or private research centers.

L'archive ouverte pluridisciplinaire **HAL**, est destinée au dépôt et à la diffusion de documents scientifiques de niveau recherche, publiés ou non, émanant des établissements d'enseignement et de recherche français ou étrangers, des laboratoires publics ou privés.

Advanced age remains an Achilles heel for liver resections.

Laurent Sulpice, MD^{1,3}, Michel Rayar, MD¹, , Boris Campillo, MD², Claire Pery MD¹, Antoine Guillaud, MD¹, Bernard Meunier, MD¹ and Karim Boudjema, MD, PhD^{1,3}

- 1- Service de Chirurgie Hépatobiliaire et Digestive. Centre Hospitalier Universitaire de Rennes, Université de Rennes 1, France
- 2- INSERM, UMR936, Département d'Information Médicale, Université de Rennes 1, France
- 3- INSERM, UMR991. Foie, métabolisme et cancer. Université de Rennes1, France

Running title: Liver resection in elderly patients

Key words: Liver resection, elderly patients, mortality

Correspondence

Docteur Laurent Sulpice

Service de Chirurgie Hépatobiliaire et Digestive, Hôpital Pontchaillou, Centre Hospitalier Universitaire, Université de Rennes 1, Rennes, France

Email : laurent.sulpice@chu-rennes.fr

Telephone: + 33 2 99 28 84 98

Fax: + 33 299 28 41 29

Word count: 2449

Conflicts of interest: The authors have no conflicts of interest to declare

Funding: The study received no external support

Author contributions: LS conceived and designed study, undertook the analysis and interpretation of data, and wrote and finalized the manuscript. CP collected data and undertook interpretation of data. BC provided the statistical analysis. MR revised the manuscript, AG collected data and proof-read the manuscript. BM revised the manuscript. KB revised the manuscript and gave final approval for publication.

ABSTRACT

Background: As general population is aging, surgery in elderly patients become a major public health issue. This basic question is especially true for liver resection (LR). The aim of this study was to evaluate the operative risks of LR in elderly.

Method: Retrospective analysis of a large recent and monocentric database of LR performed between January 1, 2005 and May 31, 2011. Patients were categorized into 3 groups (<60, 60 to 74 and ≥75 years old) to analyze postoperative outcomes as well as 1-year mortality. Clinicopathological factors likely to influence outcomes were assessed by univariate and multivariable analysis.

Results: 1001 consecutive LR were performed in 912 patients (mean age 62±13 years). The distribution of the LR was 372 (37.2%), 477 (47.6%) and 152 (15.2%) in patients <60 y, 60 to 74 y and ≥75 y old, respectively. The overall morbidity and mortality rates were 33.3% and 2.5%, respectively. An age ≥75 years was independently associated with postoperative mortality (OR 4.75 (95%CI [1.5; 15.1]; p=0.008) and 1-year mortality OR 2.8 (95%CI [1.2; 6.6]; p=0.015), while the rate of postoperative complications (p=0.216), even major complications (p=0.09), was not increased. The other independent risk factors of mortality were a cirrhotic liver (p=0.017), preoperative arterial chemoembolization (p=0.001), caval vein clamping (p=0.001) and intraoperative blood transfusion (p=0.044).

Conclusion: Age beyond 75 years represent a risk factor of death after LR and should be avoided after chemoembolization or in cirrhotic patients. A specific assessment using geriatric indexes might be the key to success in this population.

INTRODUCTION

Liver resection (LR) is the most suitable curative treatment for multiple benign and malignant liver diseases. With recent advances in surgical techniques, perioperative management and postoperative care, LR has become increasingly common, and the risks associated with this major procedure have decreased. In Western countries, increased longevity leads to subsequent increasing indications for liver resection in elderly patients.

Recently, an editorial in Lancet (1) emphasized the need to provide the same care to elderly patients and younger patients whenever possible. Many papers have reported the absence of differences between elderly and younger patients in terms of postoperative morbidity and mortality.(2;3)

During the last decades, the definition of 'elderly' has evolved. While patients aged less than 60 yrs old are nowadays considered to be young, most of the studies dealing with the impact of age on postoperative outcome have focused on the 60-75 yrs interval. Geriatricians now consider 75 years to be the age over which elderly and geriatric management starts.(4) In this setting, the feasibility and benefits of LR in elderly patients remain unclear, due to small sample sizes and the wide period of analysis. While some reports showed higher postoperative mortality and morbidity rates related to age (5;6), others were unable to demonstrate any increasing morbidity or mortality after LR related to aging,(7) especially when the indication of LR was colorectal metastases(8) (CRM) or hepatocellular carcinoma(9).

The aim of this study was to analyze the outcomes after LR including the 1-year mortality in a large recent and monocentric series of patients with a special focus on age. Secondary objectives were to identify predictors of postoperative mortality that may be corrected preoperatively to decrease the risks of postoperative complications after LR in elderly patients.

PATIENTS AND METHODS

Patients

The study population included all of the consecutive liver resections (LR) without biliary anastomosis that were performed at a single tertiary referral center between January 2005 and May 2011. The clinical data were retrospectively collected from a liver resection database and analyzed after Institutional Review Board approval was obtained. (Opinion n° 12-60)

Preoperative assessment, surgical procedure and perioperative care

Before surgery, each patient was evaluated by a thoracoabdominopelvic computed tomography (CT) scan with intravenous contrast. A measure of the future liver remnant volume (LRV) was performed when required, and portal vein embolization was performed when the LRV/Total liver volume ratio was < 35%. For malignant diseases, patients were considered to be curable if the tumors could be resected with macroscopically negative surgical margins.

All LR were performed as open or laparoscopic procedures by senior hepatic surgeons. Continuous or intermittent pedicle clamping (Pringle maneuver), or selective clamping of the pedicles for the segment to be resected, was performed in most cases. Two closed-suction drains were placed in the resection space and removed on the fifth post-operative day (POD) when drainage was minimal, serous and non-bilious.

The resections were categorized according to the International Hepato-Pancreato-Biliary Association classification for liver resections ((IHPBA, Brisbane 2000) i.e. resection of (i) two or less, (ii) three and four or (iii) more than four segments were defined as (i) minor (including wedge resection) (ii) major or (iii) extended hepatectomies, respectively.(10)

All patients received antibiotic prophylaxis. A daily subcutaneous injection of low-molecular-weight heparin sodium was started as a prophylactic against deep venous thrombosis on POD 1.

Collected data

The preoperative data included general patient characteristics (age, sex and BMI score, cirrhosis), prior surgical history and primary tumor histopathology.

The perioperative data consisted of the operation duration, pedicle clamping or selective clamping of the pedicles for vascular resection when needed, vena caval clamping, concomitant abdominal surgery, and transfusion needs.

The postoperative data included the hospital length of stay (HLS), need for intensive care, reoperations, and rehospitalization. Liver failure was defined by the “50-50” syndrome on postoperative day 5 (including serum bilirubin >50 µmol/L and prothrombin time <50%).(11)

Postoperative complications were assessed and classified according to the Clavien-Dindo classification system.(12) Major complications were categorized as grades III-V and were defined as morbidity requiring radiological or surgical intervention. Postoperative mortality was defined as death occurring during the initial hospital stay or within 30 days after surgery if the patient was discharged. The 1-year post-operative mortality was also assessed.

Statistical analysis

Statistical analyses were performed with SPSS Statistics 17.0 software for Windows (SPSS Inc., Chicago, IL).

Data from the study population were described either by means and standard deviations or by absolute and relative frequencies, for quantitative and qualitative data, respectively.

To determine the cut-off over which mortality (perioperative and 1-year) was increased, accuracy curves were realized.

To evaluate the cut-off over which mortality and morbidity were increased, we pooled the patients in 3 groups: Less than 60 yrs, 60 to 74 yrs and 75 yrs old or older. Patient characteristics, perioperative parameters and outcomes were compared between the 3 groups.

The Chi square test or the Fisher exact test were used to compare qualitative data and the Student's t-test was used to compare quantitative data between groups.

The perioperative and 1-year mortality were studied according to the patient characteristics, including age before liver resection, and perioperative factors. A univariate analysis was performed with the Chi-square test or the Fisher exact test when necessary. Factors associated with death with a p value < 0.2 were tested in a multiple logistic regression model using the forward selection procedure and the Wald test to assess their independent correlation with mortality.

RESULTS

Demographic and operative data

Between January 2005 and May 2011, 1001 consecutive liver resections were performed in 912 patients (626 men and 286 women). The mean age at the time of resection was 62 ± 13 years. Two, three, four, or five successive resections were performed in 70, 6, 1 and 1 patients, respectively. Among the LR, 504 (50.3%) were performed for liver metastasis, 375 (37.5%) and 122 (12.2%) for primary liver malignant tumor and benign lesion respectively. The indications for LR are reported in table 1.

The demographic characteristics and operative data in the <60, 60 to 74 yrs, and ≥ 75 age groups are reported in Table 2. One hundred and fifty two patients were ≥ 75 yrs (15.2%); in this group, patients had a significantly lower BMI and cirrhotic livers were less frequent.

Postoperative mortality (table 3)

The overall postoperative mortality rate was 2.6 %. The distribution of mortality according to the 3 age groups is shown in Figure 1(A). The cutoff of age over which perioperative mortality was increased, was represented in figure 2. Among the 15 factors assessed by the univariate analysis, age ≥ 75 years ($p=0,045$), cirrhosis ($p=0,008$), preoperative chemotherapy ($p=0,015$), preoperative arterial chemoembolization ($p<0,001$), preoperative portal vein embolization ($p=0,005$), primary cancer ($p=0,015$), major hepatectomy ($p=0,005$), caval vein clamping ($p=0,006$) and intraoperative blood transfusion ($p=0,013$) were significantly related to postoperative mortality. On the multivariable analysis, intraoperative blood transfusion (OR=2.4; confidence interval (CI) 95% [1; 5.5]; $p=0.044$), cirrhotic liver (OR=3.3; CI 95% [1.2; 8.9]; $p=0.017$), age ≥ 75 yrs (odds ratio [OR] 4.75; [CI] 95% [1.5; 15.1]; $p=0.008$), preoperative arterial chemoembolization (OR=5.5; CI 95% [2; 15.3]; $p=0.001$), and intraoperative caval vein clamping (OR=6.1; CI 95% [2.1; 17.5]; $p=0.001$) remained significant independent risk factors for postoperative death.

Postoperative complications (tables 4 and 5)

The overall morbidity rate was 33.3%, without a significant difference between the 3 age groups ($p=0,216$). There was no significant difference between the 3 groups ($p=0,269$) in the postoperative complications according to the Clavien-Dindo classification (table 4).

Except for the hospital stay ($p=0,02$), there were no significant differences between the three groups, regarding the type of complications (table 5).

1-year mortality (table 6)

The overall 1-year mortality rate was 5.5%. The distribution of 1-year mortality according to the 3 groups of age is shown in figure 1(B). In the univariate analysis, age ≥ 75 years ($p=0.018$), sex (male, $p=0.012$), cirrhosis ($p<0.001$), preoperative chemotherapy ($p=0.024$), preoperative arterial chemoembolization ($p=0.004$), portal vein embolization ($p=0.01$), primary cancer ($p<0.001$), major hepatectomy ($p<0.001$) and intraoperative blood transfusion ($p=0.001$) were significantly associated with an increased 1-year mortality. In the multivariate analysis, age ≥ 75 years (OR 2.8; CI 95% [1.2; 6.6]; $p=0.015$), cirrhosis (OR=2.6; CI 95% [1.2; 5.6]; $p=0.013$), preoperative arterial chemoembolization (OR=5.5; CI 95% [2; 15.3]; $p=0.001$), primary cancer (OR=2.3; CI 95% [1.1; 4.6]; $p=0.026$), major hepatectomy (OR=3; CI 95% [1.5; 6]; $p=0.002$) and intraoperative blood transfusion (OR=2.1; CI 95% [1.1; 3.8]; $p=0.016$) remained independent predictive factors of increased 1-year mortality.

DISCUSSION

The main endpoint of the study was to analyze the impact of age on morbidity and mortality after liver resection. The results showed that ≥ 75 years of age was associated with increased postoperative and 1-year mortality. Preoperative portal vein embolization, chemoembolization, cirrhotic liver, intraoperative blood transfusion and caval vein clamping were also independent predictive factors of increased postoperative and 1-year mortality. No difference was found regarding the postoperative mortality between patients < 60 years and those aged 60 to 74 years.

Similarly, the present results show that an age over 75 years old was a predictive factor for a longer hospital stay, which is consistent with the results of Cho and colleagues.(13)

Compared with most of the previous studies, this work included a large number of patients resected by expert senior surgeons in a tertiary referral center in a short and recent period.

These results may be predictive of the reality of liver surgery in the near future. Indeed, in the beginning of the 21st century, there were approximately 600 million elderly people worldwide, which is three times more than 50 years ago. Within the same period, the elderly population has been aging, with an increasing rate of people ≥ 80 years old.(14) Due to these changing demographics, the elderly now account for $> 60\%$ of all new cancer cases and $> 70\%$ of cancer deaths.(15) This trend implies an expansion of surgical indications for increasingly older patients.

In spite of the improved outcomes observed at high volume centers due to the advances in surgical management and postoperative care, LR is still associated with an increased mortality in elderly. Our results are consistent with previously reported data showing that the mortality risk after liver resection increased from 2.9 to 6.7 times in patients aged less or more than 75 years, respectively (16). The novelty of our results was based on a higher postoperative mortality rate while postoperative morbidity according to the Clavien-Dindo classification was similar. There was no difference in liver failure or other liver-specific complications, indicating that the livers of elderly patients can tolerate surgery as well as

younger patients can, as previously described by Cook *et al* after resection of colorectal liver metastases.(17)

These results go against the idea that success in LR is linked to liver regeneration (LRG). Indeed, in the elderly, it is established that LRG is impaired (18) and delayed.(19) During aging, the liver is subjected to physiological changes such as alterations in hepatocyte morphology(20) and lower blood flow(21). These factors can reduce the liver's tolerance to ischemic damage and can lead to an alteration of liver function during LR.

The imbalance between increased mortality without increasing morbidity reflects the lower possibility of adaption and response to any stress and complications in this subpopulation of patients. Advanced age should not be regarded as an absolute contraindication to hepatic resection, but should encourage a careful selection of surgical candidates. This preoperative selection process should be based on the comorbidities and tumor type through preoperative evaluation and a close collaboration between the surgeon, anesthesiologists and geriatricians.

According to our multivariate analysis, 4 other independent risk factors for postoperative mortality were statistically significant: preoperative cirrhosis, preoperative arterial chemoembolization, caval vein clamping and intraoperative blood transfusion. These results strongly suggest that LR should be avoided in elderly patients with cirrhosis and therefore could be discussed for HCC. Nevertheless, Yamada *et al* (22) reported the short and long-term safety of LR for HCC in super-elderly patients, even those > 80 years old.(2;3;23) These results might be explained in part by the small sample size (n=11) for the super-elderly group as well as selection bias. No patient in the Yamada study had an American Society of Anesthesiologists-Physical Status (ASA-PS) score ≥ 2 . Recently, Ide *et al.* also emphasized that the mortality rate was similar in young (<75 years) and elderly (>75 years) patients with HCC.(24) They demonstrated that only surgical stress-preoperative risk score (PRS) was linked to postoperative morbidity in elderly.

Referring to our results, LR appears to be safe as long as the liver is non-cirrhotic, a situation that is associated with benign tumors or colorectal liver metastases

(CRLM).(17;25;26) Regarding the latest indication, the largest series currently published (25) reported 37.8% morbidity and 5% mortality rates, which are percentages that are comparable to our results.

Furthermore, the results showed that intraoperative blood transfusion was associated with increased postoperative mortality. These results are in line with the findings of Shiba et al.(27) Patients who received blood transfusion during LR were more likely to have a longer postoperative length of stay and Clavien Grade IIIa or more complications.(28) These data emphasize the need to minimize bleeding during LR, which may be facilitated by the management of this condition at a referral center.

The difficulty in gerontosurgery is linked to the evaluation of the physiological status of patients. Aging leads to reduced renal, hepatic, cardiopulmonary functional reserve and nutritional status. The ASA score is widely and often exclusively used, but has proven not to be sensitive enough for elderly patients undergoing major surgery.(29;30) More specific scores should be used in the elderly to better select patients before LR. Using surgery geriatric indices such as the Charlson score (31;32), Cumulative Illness Rating Scale, or Kaplan-Feinstein index (33) might lead to better appraisal of the physiological age. These geriatric indices have proven to be simple, reliable, and sensitive. Unfortunately, these factors could not be assessed in this retrospective study. Indeed, as comorbidities were not available in our liver resection database for the entire population, they could not be analyzed. This lack of data requires us to interpret our results with caution. Besides, this limitation is also encountered in other large retrospective study previously published on the same topic.(25)

In summary, from this large series of LR at one tertiary referral center of liver surgery, we have identified the cut-off age that is closely correlated with an increased risk of mortality. An age over 75 years was independently associated with increased postoperative and 1-year mortality while postoperative morbidity, especially major complications, was not affected. These results may be explained by the loss of responsiveness to stress and complications

related to age. A careful selection of elderly patients undergoing LR, avoiding patients with cirrhosis, and a specific assessment of the patient's general condition using geriatric indexes might be the key to success in this population.

REFERENCES

1. Ageing well: a global priority. *Lancet* 2012;379(9823)1274.
2. Poon RT, Fan ST, Lo CM, et al. Hepatocellular carcinoma in the elderly: results of surgical and nonsurgical management. *Am.J.Gastroenterol.* 1999;94(9)2460-2466.
3. Ferrero A, Vigano L, Polastri R, et al. Hepatectomy as treatment of choice for hepatocellular carcinoma in elderly cirrhotic patients. *World J.Surg.* 2005;29(9)1101-1105.
4. Arai H, Ouchi Y, Yokode M, et al. Toward the realization of a better aged society: messages from gerontology and geriatrics. *Geriatr.Gerontol.Int.* 2012;12(1)16-22.
5. Menon KV, Al-Mukhtar A, Aldouri A, et al. Outcomes after major hepatectomy in elderly patients. *J.Am.Coll.Surg.* 2006;203(5)677-683.
6. Figueras J, Ramos E, Lopez-Ben S, et al. Surgical treatment of liver metastases from colorectal carcinoma in elderly patients. When is it worthwhile? *Clin.Transl.Oncol.* 2007;9(6)392-400.
7. Riffat F, Chu F, Morris DL. Liver resection in octogenarians. *HPB (Oxford)* 2006;8(3)206-210.
8. de Liguori CN, van Leeuwen BL, Ghaneh P, et al. Liver resection for colorectal liver metastases in older patients. *Crit Rev.Oncol.Hematol.* 2008;67(3)273-278.
9. Mirici-Cappa F, Gramenzi A, Santi V, et al. Treatments for hepatocellular carcinoma in elderly patients are as effective as in younger patients: a 20-year multicentre experience. *Gut* 2010;59(3)387-396.
10. Strasberg SM. Nomenclature of hepatic anatomy and resections: a review of the Brisbane 2000 system. *J.Hepatobiliary.Pancreat.Surg.* 2005;12(5)351-355.
11. Balzan S, Belghiti J, Farges O, et al. The "50-50 criteria" on postoperative day 5: an accurate predictor of liver failure and death after hepatectomy. *Ann.Surg.* 2005;242(6)824-8, discussion.
12. Dindo D, Demartines N, Clavien PA. Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. *Ann.Surg.* 2004;240(2)205-213.
13. Cho SW, Steel J, Tsung A, et al. Safety of liver resection in the elderly: how important is age? *Ann.Surg.Oncol.* 2011;18(4)1088-1095.
14. World population ageing. New York United Nations , 35. 2002.
15. Aapro MS, Kohne CH, Cohen HJ, et al. Never too old? Age should not be a barrier to enrollment in cancer clinical trials. *Oncologist.* 2005;10(3)198-204.
16. Bentrem DJ, Cohen ME, Hynes DM, et al. Identification of specific quality improvement opportunities for the elderly undergoing gastrointestinal surgery. *Arch.Surg.* 2009;144(11)1013-1020.

17. Cook EJ, Welsh FK, Chandrakumaran K, et al. Resection of colorectal liver metastases in the elderly: does age matter? *Colorectal Dis.* 2012;14(10)1210-1216.
18. Schmucker DL. Age-related changes in liver structure and function: Implications for disease? *Exp.Gerontol.* 2005;40(8-9)650-659.
19. Sanchez-Hidalgo JM, Naranjo A, Ciria R, et al. Impact of age on liver regeneration response to injury after partial hepatectomy in a rat model. *J.Surg.Res.* 2012;175(1)e1-e9.
20. James OF. Gastrointestinal and liver function of old age. *Clin.Gastroenterol.* 1983;12(3)671-691.
21. Wynne HA, Cope LH, Mutch E, et al. The effect of age upon liver volume and apparent liver blood flow in healthy man. *Hepatology* 1989;9(2)297-301.
22. Yamada S, Shimada M, Miyake H, et al. Outcome of hepatectomy in super-elderly patients with hepatocellular carcinoma. *Hepatol.Res.* 2012;42(5)454-458.
23. Hanazaki K, Kajikawa S, Shimosawa N, et al. Hepatic resection for hepatocellular carcinoma in the elderly. *J.Am.Coll.Surg.* 2001;192(1)38-46.
24. Ide T, Miyoshi A, Kitahara K, et al. Prediction of postoperative complications in elderly patients with hepatocellular carcinoma. *J.Surg.Res.* 2013.
25. Adam R, Frilling A, Elias D, et al. Liver resection of colorectal metastases in elderly patients. *Br.J.Surg.* 2010;97(3)366-376.
26. Di BF, Berretta M, D'Amico G, et al. Liver resection for colorectal metastases in older adults: a paired matched analysis. *J.Am.Geriatr.Soc.* 2011;59(12)2282-2290.
27. Shiba H, Ishida Y, Wakiyama S, et al. Negative impact of blood transfusion on recurrence and prognosis of hepatocellular carcinoma after hepatic resection. *J.Gastrointest.Surg.* 2009;13(9)1636-1642.
28. Gruttadauria S, Saint Georges CM, Pagano D, et al. Impact of blood transfusion on early outcome of liver resection for colorectal hepatic metastases. *J.Surg.Oncol.* 2011;103(2)140-147.
29. Reddy SK, Barbas AS, Turley RS, et al. Major liver resection in elderly patients: a multi-institutional analysis. *J.Am.Coll.Surg.* 2011;212(5)787-795.
30. Sulpice L, Rayar M, D'Halluin PN, et al. Impact of age over 75 years on outcomes after pancreaticoduodenectomy. *J.Surg.Res.* 2012;178(1)181-187.
31. Charlson ME, Pompei P, Ales KL, et al. A new method of classifying prognostic comorbidity in longitudinal studies: development and validation. *J.Chronic.Dis.* 1987;40(5)373-383.
32. Buntinx F, Niclaes L, Suetens C, et al. Evaluation of Charlson's comorbidity index in elderly living in nursing homes. *J.Clin.Epidemiol.* 2002;55(11)1144-1147.
33. Extermann M. Measuring comorbidity in older cancer patients. *Eur.J.Cancer.* 2000;36(4)453-471.

TABLE LEGENDS

Table 1. The indications for liver resections according to the patient age.

Table 2. The demographic characteristics and surgical data according to the patient age.

Table 3. The risk factors for postoperative mortality.

Table 4. The postoperative complications according to the patient age.

Table 5. The type of postoperative complications according to patient age.

Table 6. The risk factors for 1-year mortality.

FIGURE LEGEND

Figure 1. The impact of age on mortality. (A) perioperative mortality and (B) 1-year mortality.

Figure 2. Accuracy curve showing impact of age in mortality

Table 1. The indications for liver resections according to the patient age

	Age (years)		
	< 60 n=372 (%)	60 to 74 n=477 (%)	>75 n=152 (%)
Liver metastases	200 (53.8)	237 (49.7)	67 (44.1)
Primary tumors	75 (20.1)	205 (43)	64 (42.1)
Benign tumor	97 (26.1)	35 (7.3)	21 (13.8)

Table 2 . The demographic characteristics and surgical data according to the patient age.

Parameter		Age (years)			p value
		< 60 (n=372)	60 to 74 (n=477)	>75 (n=152)	
Gender	male	59.1%	75.9%	66.4%	<0.001
	female	40.9%	24.1%	33.6%	
BMI	<25	46.2%	26.2%	33.6%	<0.001
	25 to 30	41.4%	57.4%	54.6%	
	>30	12.4%	16.4%	11.8%	
Cirrhosis	no	91.4%	84.7%	90.1%	0.008
	yes	8.6%	15.3%	9.9%	
Portal vein embolization	no	90.3%	85.7%	94.7%	0.005
	yes	9.7%	14.3%	5.3%	
Type of resection	minor	48.1%	44.9%	45.4%	0.627
	major	51.9%	55.1%	54.6%	
Type of clamping					0.446
	selective	9.4%	11.5%	7.9%	
	pedicular	71.2%	72.3%	76.3%	
Caval vein clamping					0.278
	no	92.2%	93.3%	96.1%	
	yes	7.8%	6.7%	3.9%	
Perioperative radiofrequency	no	93.3%	96.2%	97.4%	0.056
	yes	6.7%	3.8%	2.6%	
Associated colorectal resection	no	92.5%	92.5%	93.4%	0.917
	yes	7.5%	7.5%	6.6%	
Associated vascular resection	no	97.6%	98.7%	96.7%	0.227
	yes	2.4%	1.3%	3.3%	

Table 3. The risk factors for postoperative mortality.

Parameter	Univariate			Multivariable		
		Alive n (%)	Died n (%)	P value	Odds Ratio (95%CI)	p value
Age (years)	<60	366 (37.5)	6 (23.1)	0.045	1.000	-
	60 to 74	465 (47.7)	12 (46.2)		1.468 (0.518-4.154)	0.470
	≥75	144 (14.8)	8 (30.7)		4.751(1.498-15.066)	0.008
Gender	male	661 (67.8)	22 (84.6)	0.069		
	female	314 (32.2)	4 (15.4)			
BMI	<25	341 (35)	7 (26.9)	0.554		
	25 to 30	495 (50.8)	16 (61.5)			
	≥30	139 (14.2)	3 (11,6)			
Cirrhosis	no	863 (88.5)	18 (69.2)	0.008	1.000	-
	yes	112 (11.5)	8 (30.8)		3.314 (1.234-8.900)	0.017
Preoperative chemotherapy	no	549 (56.3)	22 (84.6)	0.015		
	old	63 (6.4)	1 (3.9)			
	recent*	363 (37.3)	3 (11.5)			
Preoperative arterial chemoembolization	no	932 (95.6)	19 (73.1)	<0.001	1.000	-
	yes	43 (4.4)	7 (26.9)		5.487 (1.969-15285)	0.001
Portal vein embolization	no	871 (89.3)	18 (69.2)	0.005		
	yes	104 (10.7)	8 (30.8)			
Type of tumor	metastases	498 (51.1)	6 (23.1)	0.015		
	Primary cancer	329 (33.7)	15 (57.7)			
	Benign tumor	148 (15.2)	5 (19.2)			
Surgical approach	laparotomy	933 (95.7)	26 (100)	0.622		
	laparoscopy	42 (4.3)	0 (0)			
Type of resection	minor	457 (46.9)	5 (19.2)	0.005		
	major	518 (53.1)	21 (80.8)			
Type of clamping	selective	99 (10.2)	3 (11.5)	0.76		
	pedicular	706 (72.2)	20 (77)			
	no	170 (17.6)	3 (11.5)			
Caval vein clamping	no	914 (93.7)	20 (76.9)	0.006	1.000	-
	yes	61 (6.3)	6 (23.1)		6.103 (2.121-17.514)	0.001
Associated colorectal resection	no	904 (92.7)	23 (88.5)	0.433		
	yes	71 (7.3)	3 (11.5)			
Associated vascular resection	no	955 (97.9)	26 (100)	1		
	yes	20 (2.1)	0 (0)			
Intraoperative blood transfusion	no	762 (78.2)	15 (57.7)	0.013	1.000	-
	yes	213 (21.8)	11 (42.3)		2.361 (1.023-5.449)	0.044

*recent defined chemotherapy performed within 6 months before surgery.

Table 4. The postoperative complications according to the patient age.

		<i>Age (years)</i>			p value
		< 60 n=372 (%)	60 to 74 n=477 (%)	>75 (n=152)	
Postoperative complication	no	242 (65.1)	292 (61.2)	87 (57.2)	0.216
	yes	130 (34.9)	185 (38.8)	65 (42.8)	
Clavien classification grade of complications	I	24 (6.4)	24 (5)	13 (8.6)	0.269
	II	46 (12.4)	84 (17.6)	25 (16.4)	
	IIIa	24 (6.4)	29 (6.1)	8 (5.3)	
	IIIb	21 (5.6)	20 (4.2)	6 (3.9)	
	IVa	8 (2.2)	11 (2.3)	5 (3.3)	
	IVb	1 (0.3)	5 (1)	0 (0)	
	V	6 (1.6)	12 (25.2)	8 (5.3)	

Table 5. The type of postoperative complications seen according to patient age

Parameter	Age (years)			p value
	< 60 (n=372) n (%)	60 to 74 (n=477) n (%)	>75 (n=152) n (%)	
Liver failure	10 (2.7)	12 (2.5)	7 (4.6)	0.39
Postoperative ascites	14 (3.8)	25 (5.2)	2 (1.3)	0.10
Biliary leak/fistula	27 (7.3)	45 (9.4)	8 (5.3)	0.21
Postoperative hemorrhage	18 (4.8)	11 (2.3)	8 (5.3)	0.08
Intra-abdominal abscess	24 (6.5)	16 (3.4)	6 (3.9)	0.09
Wound infection	2 (0.5)	5 (1)	2 (1.3)	0.62
Systemic infection	28 (7.5)	40 (8.4)	13 (8.6)	0.88
Pulmonary Complication	20 (5.4)	35 (7.3)	10 (6.6)	0.52
Urinary complication	9 (2.4)	15 (3.1)	4 (2.6)	0.81
Deep venous thrombosis	7 (1.9)	7 (1.5)	1 (0.7)	0.58
Major complications	59 (15.9)	76 (15.9)	27 (17.8)	0.09
Hospital stay (days)†	10.8 ± 7.4	12 ± 9.2	13± 8.2	0.02

† Mean ± Standard deviation (SD)

Major complications are defined as Clavien group ≥ III.

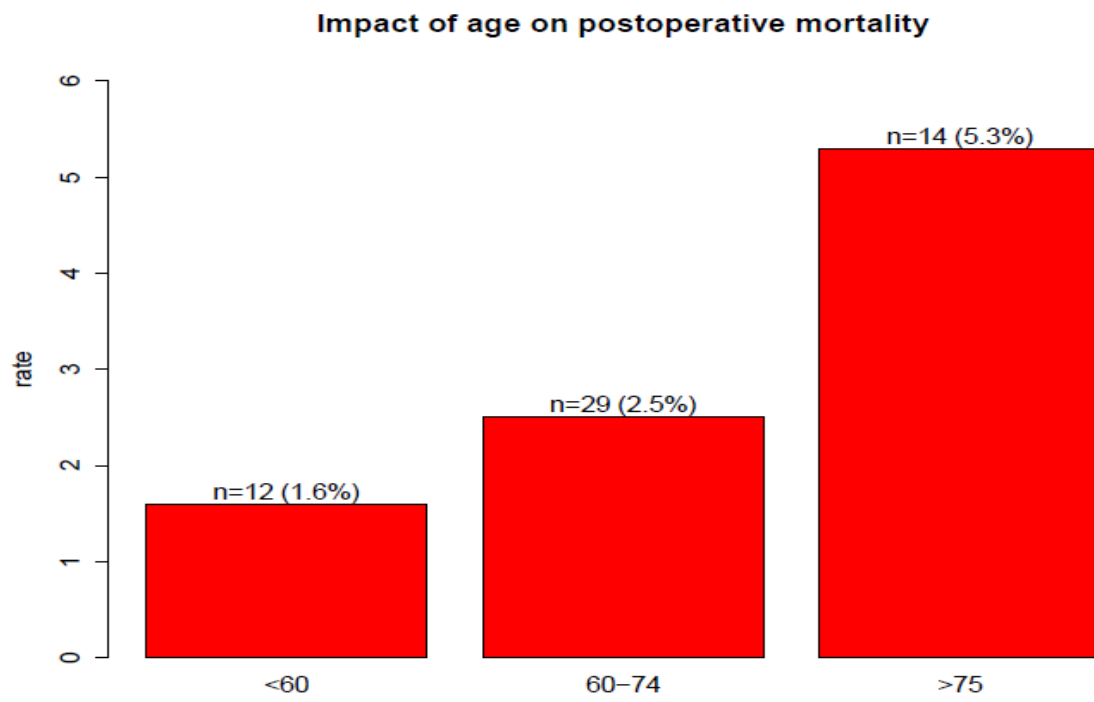
Table 6. The risk factors for 1-year mortality.

Parameter	Univariate			Multivariate	
	Alive n (%)	Died n (%)	p value	Odds Ratio (95%CI)	p value
Age (years)	<60	360 (38)	12 (21.8)	1.000	-
	60 to 74	448 (47.4)	29 (52.7)	1.636 (0.787-3.403)	0.188
	≥75	138 (14.6)	14 (25.5)	2.838 (1.223-6.584)	0.015
Sex	male	637 (67.3)	46 (83.6)		
	female	309 (32.7)	9 (16.7)		
BMI	<25	334 (35.3)	14 (25.5)		
	25 to 30	477 (50.4)	34 (61.8)		
	≥30	135 (14.3)	7 (12.7)		
Cirrhosis	no	841 (88.9)	40 (72.7)	1.000	-
	yes	105 (11.1)	15 (27.3)	2.628 (1.229-5.620)	0.013
Preoperative chemotherapy	no	530 (56)	41 (74.6)		
	old	62 (6.6)	2 (3.6)		
	Recent*	354 (37.4)	12 (21.8)		
Preoperative arterial chemoembolization	no	904 (95.6%)	47 (85.5)	1.000	-
	yes	42 (4.4)	8 (14.5)	5.487 (1.969-15.285)	0.001
Portal vein embolization	no	846 (89.4)	43 (78.2)		
	yes	100 (10.6)	12 (21.8)		
Type of tumor	metastases	489 (51.7)	15 (27.3)	1.000	-
	Primary cancer	311 (32.9)	33 (60)	2.266	0.026
	Benign tumor	146 (15.4)	7 (22.7)	1.753	0.246
Surgical approach	laparotomy	904 (95.7)	55 (100)		
	laparoscopy	42 (4.3)	0 (0)		
Type of resection	minor	450 (47.6)	12 (11.8)	1.000	-
	major	496 (52.4)	43 (78.2)	3.019 (1.516-60.15)	0.002
Type de clamping	selective	98 (10.4)	4 (6.3)		
	pedicular	683 (72.2)	43 (78.2)		
	no	165 (17.4)	8 (14.5)		
Caval vein clamping	no	886 (93.7)	48 (87.3)	1,000	-
	yes	60 (6.3)	7 (22.7)	2.301	0.069
Associated colorectal resection	no	876 (92.6)	51 (92.7)		
	yes	70 (7.4)	4 (7.3)		
Associated vascular resection	no	927 (98)	54 (98.2)		
	yes	19 (2)	1 (1.8)		
Intraoperative blood transfusion	no	744 (78.6)	33 (60)	1.000	-
	yes	202 (21.4)	22 (40)	2.078 (1.149-3.759)	0.016

*recent defined chemotherapy performed within 6 months before surgery

Figure 1

(A)



(B)

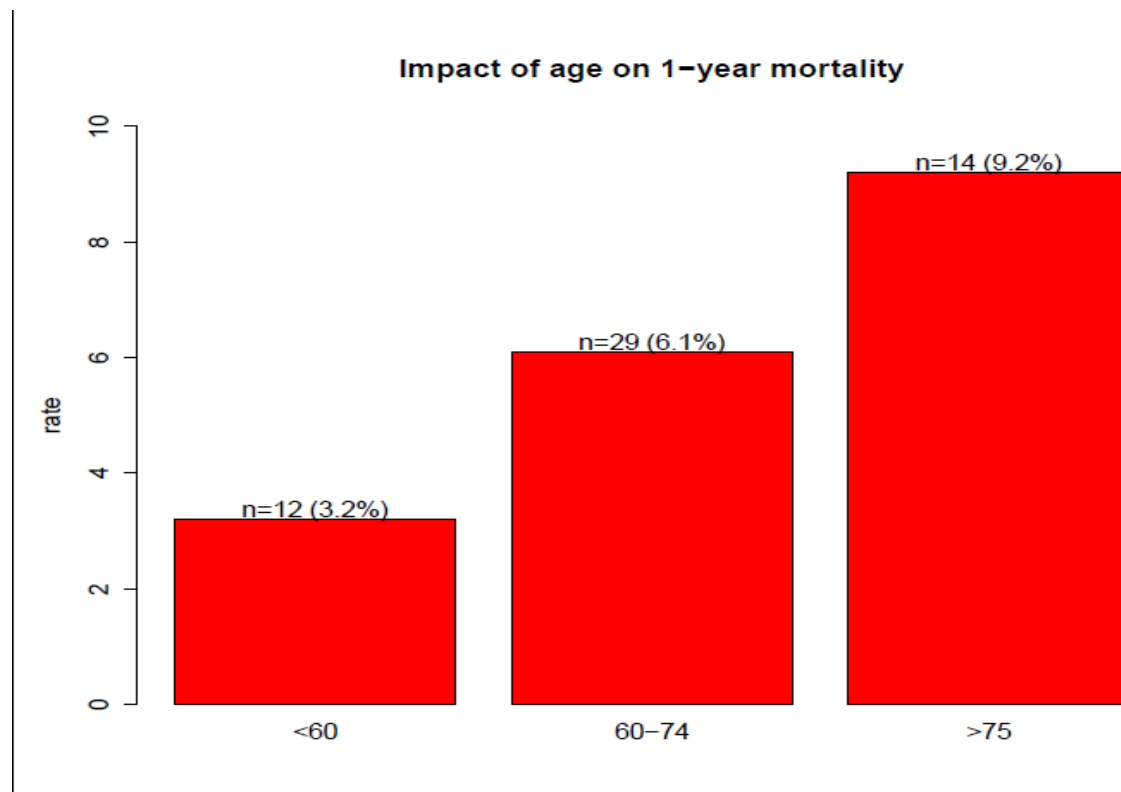


Figure 2

