Validity of hepatic resection for cancer in the elderly

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Abstract

This retrospective review assessed the safety and validity of elective hepatic resection for cancer in patients ≥65 years of age. Fifty-two patients (31M; 21F; mean age: 70±5 years; range: 65-82) ≥65 years of age underwent hepatic resection for cancer between January 1992 and May 1999). The overall peroperative mortality rate was 8%. The mean hospital stay was 23±10 days (range: 6-45 days), and admission to the intensive care unit was required for only 1 patient. By univariate analysis, preoperative jaundice (p=0.03), length of surgery (≥240 min.) (p=0.006), peroperative blood transfusions (≥500 cc) (p=0.001), and extent of hepatic resection (p=0.01), were predictors of postoperative complications. In a multivariate analysis only peroperative blood transfusions predicted complications (p=0.01). When outcome was compared with that in 65 patients younger than 65 years of age who had hepatic resection for cancer during the same period, there were no difference in terms of morbidity, mortality, and mean hospital stay The 1-, 3-, and 5-year survival rate for patients ≥65 years of age and for patients <65 years of age were 89%, 61%, and 45%, and 87%, 46% and 39% respectively. Hepatic resections can be performed for the elderly with acceptable morbidity and mortality rates and possible long-term survival. Chronological age alone is not a contraindication to liver surgery for malignancies.

Key words: Liver resection, age, survival.

Riassunto

RESEZIONE EPATICA CURATIVA PER CANCRO NEL PAZIENTE ANZIANO

Cinquantadue pazienti (31 M; 21 F; età media: 70±5; range: 65-82) con età ≥65 anni ed affetti da neoplasia maligna del fegato, sono stati sottoposti a resezione epatica nel periodo compreso tra il Dicembre 1992 e il Maggio 1999. La mortalità peroperatoria registrata è stata dell' 8%. La degenza media osservata è stata di 23±10 giorni (range: 6-45) ed un solo paziente ha richiesto il ricovero in unità di terapia intensiva. Dall'analisi univariata l' ittero preoperatorio (p=0.03), la durata dell' intervento chirurgico (≥240 min.) (p=0.006), l'emotrasfusione peroperatoria (≥500 cc) (p=0.001) ed il tipo di intervento chirurgico (p=0.01), sono risultati associati ad una maggiore incidenza

Introduction

Favourable results in young patients have encouraged the use of hepatic resection in all patients with liver cancer, but the stress of liver resection may not be well tolerated in the elderly (1, 2). This is important because the high prevalence of liver cancers and the ageing of the world population have combined to increase the elderly patients considered for hepatic resection. Fortner and Lincer (3) reported an 11% mortality rate in patients aged over 64 years, and Yanaga et al. (4) a rate of 41% for elderly patients with hepatocellular carcinoma. Ezaki et al. (5) showed that mortality in patients older than 66 years was due to intraoperative blood loss and postoperative hepatic failure.
In this study the validity of curative hepatic resection for cancer and other risk factors associated with this type of surgery, were analyzed in a consecutive series of elderly patients.

Patients and methods

Between January 1992 and May 1999 a consecutive series of 52 hepatic resections for cancers were performed at the Department of Emergency Surgery at the University of Milan - San Raffaele Hospital. Data collected included sex, age, diagnosis, preoperative grading using the

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di complicanze post-operatorie. Dall'analisi multivariata solo le emotrasfusioni peroperatorie (p=0.01) sono risultate correlate ad una maggiore incidenza di complicanze post-operatorie. Non è stata registrata alcuna differenza statisticamente significativa in termini di morbidità, mortalità e degenza peroperatoria in rapporto ad una serie consecutiva di 65 pazienti con età <65 anni affetti da neoplasia maligna del fegato e sottoposti a resezione epatica nel corso dello studio. La sopravvivenza registrata ad 1-, 3-, e 5 anni per i pazienti con età ≥65 anni e per i pazienti con età <65 anni è risultata dell' 89%, 61% e 45% e dell' 87%, 46% e 39% rispettivamente. La resezione del fegato nel paziente anziano costituisce quando possibile il trattamento terapeutico di scelta offrendo una morbilità ed una mortalità peroperatorie accettabili. L'età non deve costituire a priori una controindicazione alla chirurgia resettiva del fegato.
Parole chiave: Resezione epatica, età, sopravvivenza.

criteria established by the American Society of Anaesthesiologists (ASA) (6), type of surgery, peroperative blood transfusion, morbidity, peroperative mortality (within 30-day following surgery), and duration of hospitalization. The extent of hepatectomy was classified according to Couinaud (7).
Liver functional reserve for cirrhotic patients was assessed by the Child-Pugh classification (8).
Routine follow-up was performed every 4 months for 2 years and every 6 months thereafter.
The data from 52 patients were compared with those from 65 patients aged less than 65 years who had hepatic resection for cancer during the same period.

Statistical analysis

Chi-square test or Fisher's exact test were used for univariate analysis. Multiple logistic regression analysis was used to incorporate all of the explanatory variables in the same model (9).
Survival rates were calculated and compared according to the Kaplan-Meier method (10).
A p values less than 0.05 was considered statistically significant.
The data were expressed as the mean ±SD.

Results

Fifty-two patients over 65 years of age (31 men and 21 women; mean age: 70±5 years; range: 65-82 years) had hepatic resection for cancer in this study.
Twenty six patients (50%) had liver resection for hepatocellular carcinoma (HCC), and 22 patients (42%) for metastases from colorectal cancer.
There were 10 major hepatic resections (three or more segments removed) with 3 postoperative deaths (30%) (two patients with hepatic failure, one of them for hepato-renal syndrome, and one patient as a consequence of myocardial infarction). Forty-one minor hepatic resections were performed with one death from hepatic failure. Indications for surgery and type of operation performed are listed in Table I (a-b).
Histopathologically proven cirrhosis was diagnosed in 26 patients (50%), with 3 patients (6%) showing fatty infiltration and fibrosis remote from the tumour.
The liver resections were performed with Pringle manouvre in 44 patients (85%) (11).
In 8 cirrhotic patients (15%) hepatic resections were performed with the hemihepatic vascular occlusion technique (HVO) (12). No patients underwent complete vascular exclusion.
Of the 73 neoplastic lesions, 14 tumours were multiple. The median number of tumours in patients presenting

Tab. Ia – CHARACTERISTICS OF ELDERLY PATIENTS UNDERGOING HEPATIC RESECTION

	Major resection n=10	*Minor resection n=42*
Mean age	70	70
Sex ratio (M : F)	5 : 5	26 : 16
Diagnosis		
HCC	4	22
Gallbladder cancer	1	1
Cholangiocarcinoma	1	-
Colonic metastases	4	18
Other metastases	-	1
Associated medical conditions		
Cardiovascular	5	14
Previous MI	-	6
Angina	1	1
Arrhytmia	-	1
Pulmonary	-	1
Diabetes	2	3
Cirrhosis	4	22

HCC, hepatocellular carcinoma;
MI, myocardial infarction.

Tab. Ib – HEPATIC RESECTIONS IN PATIENTS ≥65 YEARS OF AGE

	N° of patients n=52
Major hepatic resection	
Left hepatectomy	1 (2)
Right hepatectomy	9 (17)
Minor hepatic resection	
Bisegmentectomy	8 (15)
Segmentectomy	14 (27)
Wedge resection	20 (39)

Values in parentheses are percentages.

with multiple lesions was 2 (range: 2-4). Median size of the tumours was 3.3 centimeter in maximal diameter (range: 0.4-15 cm).

The mean peroperative blood loss was 713±542 cc (range: 100-2000 cc) and the mean duration of hospital stay was 23±10 days (range: 6-45 days). The overall peroperative mortality rate was 8% (n=4) and for extended major hepatectomy was 30% (n=3). The overall complication rate was 33% (n=17), which included abdominal abscesses in 11% (n=6), cardiopulmonary complications in 6% (n=3), and liver failure in 6% (n=3) (Table II).

Only one patient required postoperative admission to the intensive care unit.

With so few peroperative deaths, analysis for predictors of death was not performed.

Univariate analysis revealed that a bilirubin level above 2.0 mg/dL (N.V.: <1.00 mg/dL), a duration of operation greater than 240 minutes, peroperative blood transfusions (500 cc or more), and extent of hepatic resection (≥3 segments removed), were predictors of postoperative complications (Table III).

History of cardiac disease or cirrhosis was not predictive of complications.

Extent of hepatic resection, peroperative blood transfusions, and time of operation, were used as covariables in a multivariate analysis of predictors of complications following hepatic resection in these patients. Because jaundice was found in only three patients, this was not entered as a variable. By multiple logistic regression analysis, only a peroperative blood transfusions (500 cc or more) was predictive for postoperative complications (Table IV) (p=0.01).

When the mortality and morbidity data were analysed separately for age cohorts of 65-69, 70-74 and 75 years or more, no significant differences between these three groups were found.

During the 89 months of this study, 66 patients under 65 years of age underwent hepatic resection at the same institution. Eighteen major hepatic resections, and 48 minor hepatic resections or non-anatomical (wedge) resections were performed. Liver resections were performed for colorectal metastases in 34 patients (51%), HCC in 26 cases (40%), cholangiocarcinoma in 2 (3%), gallbladder cancer in 2 (3%), and for other hepatic metastases in 2 cases (3%).

The younger patients had a mean hospital stay of 22±10 days (range: 5-57 days) while in those patients aged 65 years or more the mean hospital stay was 23±10 days (range: 6-45 days) (p=0.67).

Tab. II – COMPLICATIONS FOLLOWING HEPATIC RESECTION IN THE ELDERLY

	Major Hepatic resection n=10	*Minor Hepatic resection n=42*
Cardiopulmonary	2	1
Myocardial infarction	1	0
Pneumonia	1	1
Infection		
Intra-abdominal abscess	2	4
Wound infection	0	2
Gastrointestinal		
Liver failure	2	1
Haemoperitoneum	0	2
Peritonitis	1	0
Small bowel obstruction	0	1
Ascitic leak	1	1
Biliary leakage	2	1
Miscellaneous		
Wound dehiscence	1	0

Tab. III – UNIVARIATE ANALYSIS OF PREDICTORS OF COMPLICATIONS

	N° of Pts	*N° Complications*		*p*
Sex				
M	31	22	9	0.6
F	21	13	8	
Cardiac history				
No disease	43	27	16	0.1
Previous disease	9	8	1	
Jaundice				
None	49	35	14	0.03
Bilirubin level ≥2.0 mg/dl	3	0	3	
ECG				
Normal	23	17	6	0.3
Abnormal	29	18	11	
ASA				
I	5	3	2	
II	24	18	6	0.5
III	23	14	9	
Size of resection				
Minor	42	31	11	0.01
Major	10	4	6	
Duration of operation (min)				
<240	32	26	6	0.006
≥240	20	9	11	
Blood loss				
<1500 ml	42	29	13	0.3
≥1500 ml	8	4	4	
*Liver parenchyma**				
Normal	28	19	9	0.9
Abnormal	24	16	8	
Peroperative blood transfusion				
<500 ml	28	29	5	0.001
≥500 ml	15	6	11	

ECG, electrocardiogram;
ASA, American Society of Anestesiologists;
*Fibrosis, steatosis, cirrhosis.

Tab. IV – MULTIPLE LOGISTIC REGRESSION ANALYSIS FOR RISK OF COMPLICATIONS FOLLOWING HEPATIC RESECTION IN THE ELDERLY

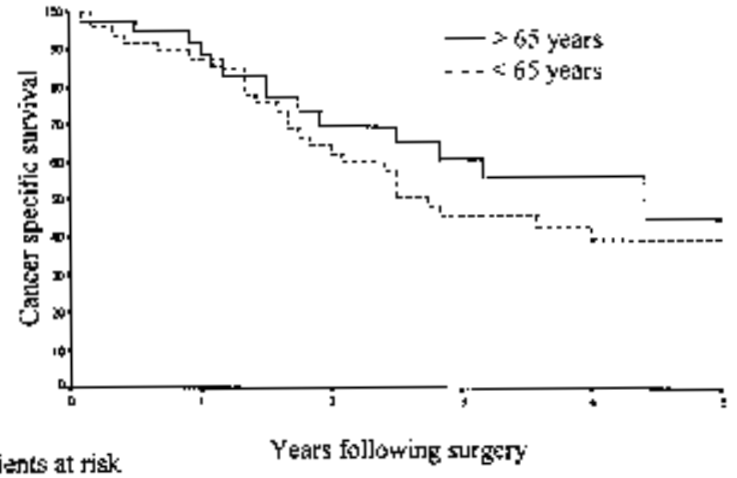
Parameter	*p*	*SE*	*Relative risk*	*95% Confidence Interval*
Duration of operation	0.12	0.8	3.4	0.7 - 15.9
Peroperative blood transfusion (≥500 ml)	0.01	0.8	7.0	1.5 - 32.2
Extent of hepatic resection (≥3 segments or <3 segments removed)	0.21	1.0	3.8	0.5 - 31.7

SE, standard error.

Survival and long-term outcome

The median follow-up for patients with 65 years or more was 23 months (range: 1-72 months). The median time to death for the 17 patients who died was 18 months whilst the median follow-up for the 31 survivors was 24 months. The 1-, 3-, and 5-year survival rates for patients with 65 years or more were 89%, 61%, and 45% respectively. The 1-, 3-, and 5-year survival rates for patients less than 65 years of age were 87%, 46%, and 39% respectively (Fig. 1) (p=0.36).

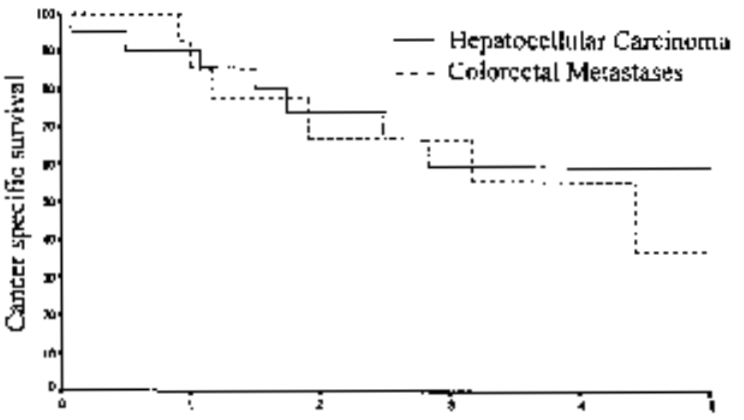
For patients ≥65 years of age who had hepatic resection for HCC and for colorectal metastases survival rates were 91%, 60%, and 60%, and 86% 67% and 37% respectively (Fig. 2) (p=0.74).



No. of patients at risk

≥ 65 years	48	37	19	13	4	3
< 65 years	59	46	33	22	14	4

Fig. 1: Overall cancer specific survival following hepatic resection for cancer. Kaplan-Meier curves are shown for patients ≥65 years of age (___) and for patients <65 years of age (- - -).



No. of patients at risk

Hepatocellular Carcinoma	23	18	10	8	3	2
Colorectal Metastases	21	15	8	6	3	1

Fig. 2: Overall cancer specific survival in patients ≥65 years of age who underwent hepatic resection for HCC (___) and for colorectal metastases (- - -).

Discussion and conclusions

Surgical therapy is the potentially curative treatment for malignant disease of the liver. The past three decades have seen a dramatic decline in the mortality rate following hepatic resection. However, this study demonstrates that major hepatic resection can be performed in patients over 65 years of age with acceptable mortality and morbidity rates, and with hospital stays comparable with other major procedures commonly performed in the elderly (13, 14).

The reported experience of hepatic resection in the aged, however, is small (1, 5, 14-17). Results have generally been poor, with operative mortality rates between 19% to 40% even though most series included only few major hepatic resections. Poor results in some series can be explained by high proportion of patients with cirrhosis (1, 3, 4), but even in studies weighted towards patients without cirrhosis, an operative mortality rate as 30% was noted for major hepatic resection in the elderly (3). Recent improvements in operative techniques and in intensive care for these patients offer improved results. In this study we report 52 patients who had liver resection in the past seven years and this demonstrates that liver resection is safe in the elderly. The major hepatic resections performed (19%) in our series, demonstrated that the elderly patients need not be denied major resection. In our experience patients have had extensive preoperative severe screening. As a result of this selection, no patients had an ASA score greater than III whereas in some surgical series reported, the ASA classification and preoperative jaundice (18, 19), are predictors of poor clinical outcome. In this study only periopertative blood transfusions was a predictors of complications in a multivariate analysis.

Both major and minor hepatic resections can be performed safely in the elderly provided they are performed on elective surgery. As with younger patients, jaundice, peroperative blood transfusions, length of surgery, and extent of hepatic resection, are factors which should be used to select suitable patients, but chronological age alone should not considered a contraindication to liver resection.

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