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ORIGINAL ARTICLE

Postoperative mortality and need for transitional care following liver resection for metastatic disease in elderly patients: a population-level analysis of 4026 patients

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Abstract

Objectives: The goal of this study was to characterize the association of age with postoperative mortality and need for transitional care following hepatectomy for liver metastases.

Methods: A retrospective cohort study using the Nationwide Inpatient Sample (2005–2008) was performed. Patients undergoing hepatectomy for liver metastases were categorized by age as: Young (aged <65 years); Old (aged 65–74 years), and Oldest (aged ≥75 years). Multivariate logistic regression analyses were performed to identify predictors of in-hospital mortality and need for transitional care (non-home discharge).

Results: A total of 4026 patients were identified; 36.6% (n = 1475) were elderly (aged ≥65 years). Rates of in-hospital mortality and non-home discharge increased with advancing age group [1.3% vs. 2.2% vs. 3.3% (P = 0.005) and 2.1% vs. 6.1% vs. 18.3% (P < 0.001), respectively]. Independent predictors of in-hospital mortality were age within the Oldest category [odds ratio (OR) 2.21, 95% confidence interval (CI) 1.19–4.12] and a Deyo Comorbidity Index score of ≥3 (OR 6.95, 95% CI 3.55–13.60). Independent predictors for need for transitional care were age within the Old group (OR 2.44, 95% CI 1.66–3.58), age within the Oldest group (OR 8.48, 95% CI 5.87–12.24), a Deyo score of 1 (OR 2.00, 95% CI 1.40–2.85), a Deyo score of 2 (OR 4.70, 95% CI 2.93–7.56), a Deyo score of ≥3 (OR 6.41, 95% CI 3.67–11.20), and female gender (OR 1.56, 95% CI 1.15–2.11).

Conclusions: Although increasing age was associated with higher risk for in-hospital mortality, the absolute risk was low and within accepted ranges, and comorbidity was the primary driver of mortality. Conversely, need for transitional care was significantly more common in elderly patients. Therefore, liver resection for metastases is safe in well-selected elderly patients, although consideration should be made for potential transitional care needs.

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Introduction

The liver is the most common site of metastatic disease.[1,2] Because of the liver's dual circulation (portal and systemic blood supplies), primary tumours that metastasize to the liver typically originate from the gastrointestinal tract, most frequently from the colon, rectum or pancreas (including neuroendocrine tumours), among other sites.[3] Up to 50% of patients with these tumours are diagnosed with metastatic liver disease, either at initial presentation or later during the course of their disease.[4] Although a multidisciplinary approach to the treatment of liver metastases is important for accomplishing optimal and comprehensive cancer care, surgical resection remains the only treatment with curative potential. For patients with colorectal liver metastases, medical treatment with systemic chemotherapy usually results in 5-year survival rates of < 5%, compared with overall survival rates of close to 60% following liver resection.[5,6] Likewise, in well-selected patients presenting with metastatic neuroendocrine tumours to the liver, liver resection results in higher survival than does medical therapy or non-operative, liver-directed interventions.[7–9] Similar results have been reported in well-selected patients treated with liver resection for metastatic disease originating from a variety of other primary tumour sites.[10,11] In tandem with improved longterm outcomes following hepatectomy, reports from national registries and high-volume centres emphasize the unquestionable improvement in the safety of hepatectomy that has occurred over the last decades; currently, mortality is reported to be < 5%[12–15] and major complications are relatively uncommon and typically temporary in nature.[12,14,15]

Despite these encouraging findings, the role of surgery in liver metastases in elderly patients has not been clearly defined.[16] Given that cancer is a disease that predominantly affects elderly people,[17] and in view of the expected sustained growth of this segment of the population, the proportion of patients with liver metastases aged > 65 years will continue to increase and surgical treatment – hepatectomy – should be part of the armamentarium for the optimal management of their disease.[16,18] Although this approach appears to be relatively intuitive, elderly patients presenting with liver metastases are often undertreated compared with younger adults;[19,20] this difference is often driven by providers' unsubstantiated perceptions of worse overall outcomes, as a result of which less aggressive diagnostic and treatment strategies are offered to older patients.[16] This treatment disparity occurs despite multiple studies reporting acceptable short-term outcomes following hepatectomy in well-selected elderly patients.[18,21–27] A major limitation of such studies, however, is that, in most cases, they represent practices within highly specialized centres, and their findings may not be applicable to other institutions. Furthermore, these studies primarily focus on postoperative mortality and complications, and thus information on the effects of liver resection on transitional outcomes in elderly patients, such as outcomes following the immediate postoperative period that represent recovery to premorbid status and quality of life following surgery, is limited. Transitional outcomes are particularly relevant in elderly patients, and postoperative and survival outcomes represent only a component of the overall treatment goals; elderly patients already have a shorter life expectancy as a result of their advanced age and associated comorbidities, and thus timely recovery and subsequent quality of life are relatively more important.[16,28]

In view of these considerations, it is unclear which elderly patients are more likely to benefit from hepatectomy in terms of postoperative and transitional outcomes following surgery. The goal of this study was to use a national database to better understand and characterize the association of increasing age with postoperative mortality and transitional outcomes following resection of secondary hepatic malignancies. Specifically, this study hypothesized that increased age would be associated with adverse outcomes after hepatic resection, but that age alone would not predict increased in-hospital mortality or need for transitional care postoperatively.

Materials and methods

Data source: Nationwide Inpatient Sample

The Nationwide Inpatient Sample (NIS) database represents approximately 20% of all community hospital discharges in the USA. It is part of the Healthcare Cost and Utilization Project, sponsored by the Agency for Healthcare Research and Quality. The NIS database incorporates over 8 million hospital stays annually and includes data on hospital and clinical information typically found in hospital discharge abstracts, thus allowing the analysis of nationwide trends in health care utilization, quality and outcomes. The NIS database was purchased for the years 2005–2008 from the Healthcare Cost and Utilization Project Central Distributor after a standard data use agreement had been completed. Data were analysed to evaluate outcomes after hepatectomy for metastatic disease in different groups of patients of increasing age.

Study sample and data collection

The NIS database was queried for all patients who underwent liver resection, using the International Classification of Disease, 9th Revision, Clinical Modification (ICD-9-CM) procedure codes 50.22 (partial hepatectomy/wedge resection of liver) and 50.3 (lobectomy or extended lobectomy of liver). Using a validated diagnostic algorithm, the study sample was limited to subjects with a diagnosis of liver metastases.[29]

Patient demographic information, including age and gender, was identified and recorded. Comorbidity was scored using the Deyo modification of the Charlson Comorbidity Index,[30] a weighted index using ICD-9-CM diagnosis codes to define the overall extent of each patient's comorbidity, including the following diagnoses: myocardial infarction; congestive heart failure; peripheral vascular disease; cerebrovascular disease; dementia; chronic pulmonary disease; connective tissue disease; ulcer disease; liver disease; diabetes; hemiplegia; renal disease; malignancy, and acquired immunodeficiency syndrome (AIDS). Similarly to previous studies,[12] cancer diagnosis and metastases were not included in the calculation of the score because these two factors were present in all patients and accounted for during the selection of the study sample. The sample was then categorized into four groups according to the severity of comorbidities (Deyo scores of 0, 1, 2 and ≥3, respectively). The sample was also categorized into two groups according to the extent of the hepatic resection using ICD-9-CM procedure codes for wedge resection (code 50.22), or lobectomy or extended lobectomy (code 50.3). Similarly, outcomes data on in-hospital mortality, length of stay (LoS) and discharge destination were identified and recorded.

Statistical analysis

The primary outcomes of interest were in-hospital mortality and poor transitional outcome, defined as the need for transitional care. Discharge destination was used as a surrogate for transitional outcome; patients discharged to a destination other than home (i.e. non-home disposition: rehabilitation, skilled nursing or longterm care facility) were considered to need transitional care. Secondary outcomes included LoS following hepatectomy. The independent variable of interest was age; patients were categorized into three different age groups: Young (aged < 65 years); Old (aged 65–74 years), and Oldest (aged ≥75 years). Baseline patient and treatment characteristics and outcomes were compared for the three groups, using the chi-squared test for categorical variables and Student's *t*-test for continuous variables. Multivariate logistic regression analyses were performed to identify independent predictors of each primary outcome and to examine the effect of increasing age while adjusting for other important variables.

Summary statistics are presented as proportions for categorical variables and as medians and ranges for continuous variables. Univariate comparisons of baseline and treatment characteristics and outcomes are reported using the *P*-value. Results of the multivariate models are presented as odds ratios (ORs) with corresponding 95% confidence intervals (CIs) and *P*-values. In all cases, a *P*-value of < 0.05 was considered to indicate statistical significance. All statistical analyses were performed using SPSS Statistics Version 17.0.0 (SPSS, Inc., Chicago, IL, USA).

Results

Patient characteristics

A total of 4026 patients who underwent hepatectomy for liver metastases were identified. Baseline patient and treatment characteristics are shown in Table 1. Over one third of patients were found to be elderly (Old or Oldest groups) and one third of elderly patients were categorized in the Oldest group. There was no difference in gender distribution among the three age groups. Notably, the severity of comorbidity rose with increasing age: most patients in the Young group (78.6%, *n* = 2005) had a Deyo Comorbidity Index score of 0 (no comorbidities), compared with 64.3% (*n* = 638) and 60.9% (*n* = 294) in the Old and Oldest groups, respectively (*P* < 0.001). Interestingly, there was no significant difference in the extent of operation among age groups.

Postoperative outcomes

There were 72 in-hospital postoperative mortalities, representing 1.8% of the whole study population. Rates of in-hospital mortality rose with increasing age from 1.3% (*n* = 34) in the Young group, to 2.2% (*n* = 22) and 3.3% (*n* = 16) in the Old and Oldest groups, respectively (*P* = 0.005). Non-home disposition was necessary in 198 patients (4.9%) and rose significantly with increasing age from 2.1% (*n* = 54) in the Young group to 6.1% (*n* = 59) in the Old group and 18.3% (*n* = 85) in the Oldest group (*P* < 0.001). Although differences among age groups in median LoS were statistically significant (*P* < 0.001), this was primarily driven by range differences without clinical relevance. Overall, median LoS was 6 days (range: 0–94 days). Bivariate analyses evaluating the effect of extent of operation (wedge resection vs. lobectomy or extended lobectomy) on each of these outcomes by age group are also depicted in Table 2.

Independent predictors of outcome

After multivariate logistic regression analysis, two independent predictors were identified for the outcome of postoperative in-hospital mortality: age within the Oldest group (OR 2.21, 95% CI 1.19–4.12; *P* < 0.001) and a Deyo score of ≥3 (OR 6.95, 95% CI 3.55–13.60; *P* < 0.001). Table 3 lists the results of this analysis with all included variables. Table 4 lists the results of the multivariate analysis performed for poor transitional outcome. Increasing age

Table 1 Baseline patient demographics and type of surgery in the entire cohort and by age group[a]

Characteristics	All patients (*n* = 4026)	Age group			*P*-value
		Young (< 65 years) (*n* = 2551)	Old (65–74 years) (*n* = 992)	Oldest (≥ 75 years) (*n* = 483)	
Gender, *n* (%)					0.160
Male	2092 (52.1%)	1297 (50.9%)	537 (54.2%)	258 (53.4%)	
Female	1929 (48.0%)	1251 (49.1%)	453 (45.8%)	225 (46.6%)	
Deyo Comorbidity Index score, *n* (%)					< 0.001
0	2937 (73.0%)	2005 (78.6%)	638 (64.3%)	294 (60.9%)	
1	793 (19.7%)	429 (16.8%)	239 (24.1%)	125 (25.9%)	
2	181 (4.5%)	71 (2.8%)	68 (6.9%)	42 (8.7%)	
≥ 3	115 (2.9%)	46 (1.8%)	47 (4.7%)	22 (4.6%)	
Surgery type, *n* (%)					0.570
Wedge resection	2663 (66.1%)	1686 (66.1%)	648 (65.3%)	329 (68.1%)	
Lobectomy	1363 (33.9%)	865 (33.9%)	344 (34.7%)	154 (31.9%)	

[a]Columns may not add to the total number for the group because some data for certain characteristics are missing. Elderly patients were more likely to have higher comorbidity scores than younger patients, but were similar in other characteristics.

Table 2 Postoperative outcomes following liver resection, by age group

Variable	Age group			*P*-value
	Young (<65 years) (*n* = 2551)	Old (65–74 years) (*n* = 992)	Oldest (≥ 75 years) (*n* = 483)	
Length of stay, days, median (range)				
All resections	6 (0–94)	7 (0–80)	7 (1–63)	<0.001
Wedge resections	6 (0–94)	6 (0–80)	8 (1–63)	<0.001
Hepatic lobectomy	6 (0–62)	7 (0–60)	7 (1–33)	<0.001
In-hospital mortality, *n* (%)				
All resections	34 (1.3%)	22 (2.2%)	16 (3.3%)	0.005
Wedge resections	18 (1.1%)	11 (1.7%)	11 (3.4%)	0.007
Hepatic lobectomy	16 (1.8%)	11 (3.2%)	5 (3.2%)	0.280
Non-home disposition, *n* (%)				
All resections	54 (2.1%)	59 (6.1%)	85 (18.3%)	<0.001
Wedge resections	37 (2.2%)	38 (6.0%)	54 (17.1%)	<0.001
Hepatic lobectomy	17 (2.0%)	21 (6.3%)	31 (20.8%)	<0.001

Length of stay after hepatectomy was slightly longer in elderly patients. Rates of in-hospital mortality and non-home disposition were significantly higher in elderly patients.

Table 3 Multivariate analysis evaluating risk factors for in-hospital mortality

Variable	Odds ratio (95% CI)	*P*-value
Age group		<0.001
Young (< 65 years)	Reference	
Old (65–74 years)	1.40 (0.80–2.45)	
Oldest (≥ 75 years)	2.21 (1.19–4.12)	
Gender		0.051
Male	Reference	
Female	0.61 (0.37–1.00)	
Deyo Comorbidity Index score		<0.001
0	Reference	
1	0.76 (0.38–1.53)	
2	1.79 (0.74–4.33)	
≥ 3	6.95 (3.55–13.60)	
Surgery type		0.070
Wedge resection	Reference	
Hepatic lobectomy	1.55 (0.97–2.50)	

Increasing age and comorbidity were independent predictors of in-hospital mortality.
95% CI, 95% confidence interval.

Table 4 Multivariate analysis evaluating risk factors for non-home discharge

Variable	Odds ratio (95% CI)	*P*-value
Age group		<0.001
Young (< 65 years)	Reference	
Old (65–74 years)	2.44 (1.66–3.58)	
Oldest (≥ 75 years)	8.48 (5.87–12.24)	
Gender		0.004
Male	Reference	
Female	1.56 (1.15–2.11)	
Deyo Comorbidity Index score		<0.001
0	Reference	
1	2.00 (1.40–2.85)	
2	4.70 (2.93–7.56)	
≥ 3	6.41 (3.67–11.20)	
Surgery type		1.000
Wedge resection	Reference	
Hepatic lobectomy	1.00 (0.73–1.37)	

Increasing age and comorbidity were independent predictors of non-home discharge.
95% CI, 95% confidence interval.

($P < 0.001$), increasing comorbidities ($P < 0.001$) and female gender ($P = 0.004$) were all identified as independent predictors of poor transitional outcome: age within the Old category, OR 2.44 (95% CI 1.66–3.58); age within the Oldest category, OR 8.48 (95% CI 5.87–12.24); Deyo score of 1, OR 2.00 (95% CI 1.40–2.85); Deyo score of 2, OR 4.70 (95% CI 2.93–7.56); Deyo score of ≥3, OR 6.41 (95% CI 3.67–11.20), and female gender, OR 1.56 (95% CI 1.15–2.11).

Discussion

Current population dynamics indicate that 20% of the population in developed countries is expected to have passed the age of 65 years by 2025.[16] In the USA, this segment of the population is projected to double from 35 million in 2000 to >70 million by 2030.[16] This demographic transition will result in an estimated doubling of the number of new cancer diagnoses to 2.6 million annually by 2050, with the most pronounced effect concerning the number of new gastrointestinal malignancies, including liver metastases originating from colorectal cancers and other primary sites.[17,31] These changes will increase the number of elderly patients requiring liver resection as part of their cancer treatment; at present, these patients are often undertreated and liver resection is avoided,[19,20] limiting any curative potential for this population. Although a series of studies have supported the safety of hepatectomy in older adults,[18,21–26,32–34] other studies have reported contradictory results.[35,36] Moreover, most studies evaluating the role of liver resection in elderly patients derive from single institutions,[22–26,32–35,37] or have used heterogeneous populations,[26,27,32,33,35,37–40] thereby limiting their generalizability. In addition, the potential impact of liver resection on elderly patients in terms of postoperative recovery and quality of life has not been studied, although it has important implications for helping to delineate the role of hepatectomy in elderly patients.

The goal of this study was to evaluate postoperative outcomes (i.e. mortality) and transitional outcomes following liver resection for metastatic disease in elderly patients using a nationwide database. The analysis revealed that although postoperative mortality is increased in older patients, it is still low and well within acceptable ranges: the present analysis found a mortality rate of 3.3% ($n = 16$) in patients aged ≥75 years. Furthermore, on multivariate analysis, the presence of multiple comorbidities (indicated by a Deyo score of ≥3) was identified as the most important predictor of postoperative mortality, and age was a significant predictor only for patients aged ≥75 years. Conversely, in terms of transitional outcomes, the need for postoperative transitional care was found to be significantly greater in patients of increasing age, reaching almost 20% ($n = 85$) in the oldest group of patients. After multivariate analysis, in addition to female gender and comorbidity status, age within the 65–74 years and ≥75 years groups were both associated with an increased risk for postoperative transitional care needs.

It is noteworthy that the postoperative mortality rate for older patients found in this study was low and well within acceptable ranges, and was similar to rates published for other younger populations.[6,14,15,41] Previous reports evaluating postoperative mortality in elderly patients have found rates in the range of 6–8%,[26,32,37,38] significantly higher than the 3.3% rate observed in the oldest group of patients (≥75 years) in this series; this discrepancy reflects a number of differences among the studies. Firstly, the population included in these studies differs from that in this report. In a study by Chiappa *et al.*,[32] the rate of post-hepatectomy mortality in 52 patients aged > 65 years was 8%; however, their population was mixed and included patients with hepatocellular carcinoma and cirrhosis. Similarly, Koperna and colleagues[37] found a significantly increased risk for mortality in patients with primary liver tumours with or without cirrhosis (23%) compared with those undergoing liver resection for metastatic disease (2.5%). Secondly, many of the studies reporting higher mortality rates have generally focused on elderly patients undergoing extensive resections or have identified major liver resections as an important predictor of mortality.[35,37,38] The present study found no difference in the distribution of more extensive resections based on age and, additionally, did not identify more extensive resection as a predictor of mortality. This difference may also reflect the inclusion of heterogeneous populations in published reports, for which postoperative outcomes are strongly linked to the liver remnant (and, hence, the extent of resection), particularly in the setting of cirrhosis. The lower mortality rate observed in the elderly population in the present study reflects, in part, a more homogeneous, low-risk group of patients (metastatic disease only) and is similar to those reported by other studies that have also limited analysis to elderly patients with metastatic disease alone.[12,18,23,34] The results of the present study emphasize the need for more homogeneous comparisons when future studies evaluating other aspects of liver resection in elderly patients are considered.

In the present series, a Deyo Comorbidity Index score of ≥3 was found to be the primary predictor of postoperative mortality and was associated with a seven-fold increase in risk for death following liver resection. This is an important finding, given the increasing number of comorbidities observed in older patients, and clarifies the association between mortality and increasing age in a select group of older patients (those with multiple comorbidities). These findings are congruent with other reports in which comorbidities have been associated with increased risk for postoperative mortality.[38–40] These studies are limited, however, by the use of non-standardized or less reliable measures of comorbidity. The utilization of a standardized and dependable approach to measuring the degree of comorbidities in the present study (the Deyo modification of the Charlson Comorbidity Index) strengthens the validity of this association.

After multivariate analysis, age of ≥75 years was also found to be an independent predictor of mortality. Two different age cut-offs were used to discriminate elderly patients, according to previous reports[42,43] and the authors' own experiences, based on the different overall physiological reserves of and clinical outcomes in younger elderly patients (aged 65–74 years) compared with the oldest patients (≥75 years). The present findings support the authors' experiences and previous reports in that the patients in the Oldest group were found to have a higher risk for postoperative mortality (OR 2.21, 95% CI 1.19–4.12). However, the overall low postoperative mortality rate observed in this high-risk group supports the use of liver resection in these patients when they are appropriately selected. Based on the findings of this study, it appears clear that comorbidity is an important factor in the selection process; however, future studies should focus on the role of more comprehensive geriatric assessments to better discriminate among those who will and will not benefit from liver resection.

This study also evaluated the effects of age on need for transitional care. Few studies have examined patient-centred outcomes such as recovery to premorbid status (i.e. transitional outcomes) and quality of life following surgery for liver metastases, although these are particularly relevant to elderly patients. A discharge destination other than home was used as a surrogate for transitional care needs and found to be directly related to increasing age; only 2.1% ($n = 54$) of patients in the Young group required transitional care, compared with 6.1% ($n = 59$) and 18.3% ($n = 85$) of patients in the Old and Oldest groups, respectively. More importantly, after multivariate analysis, in addition to female gender and increasing comorbidity, age in the 65–74 years category and ≥75 years category were both associated with a significant increase in need for transitional care [OR 2.44 (95% CI 1.66–3.58) and OR 8.48 (95% CI 5.87–12.24), respectively]. This finding adds to available data on postoperative transitional outcomes following liver resection in elderly patients. A recent study by Cho and colleagues[27] reported an important difference in rates of non-home discharge between young and older patients (1% vs. 19%, respectively). However, the study was limited by its inclusion of only rehabilitation facilities, the mixed nature of its population (primary and metastatic disease) and its failure to evaluate other potential confounding factors. Despite this, the authors[27] reported a high rate of transitional care needs in elderly patients, as in the present study. This has important implications when liver resection is offered to elderly patients; in addition to longterm survival, transitional and health-related quality of life outcomes should be included in the process of deciding whether or not hepatectomy should be performed, and patients should be counselled with regard to these potential needs. If liver resection is deemed to be appropriate following these standards, discharge planning should be coordinated early during the preoperative period in high-risk populations.

The findings of this study should be interpreted within the scope of its limitations. Its retrospective nature has important implications with regard to the selection bias associated with the cohort and limits its ability to contribute towards the defining of a standardized approach to selecting elderly patients who are likely to withstand and benefit from liver resection. However, high-risk groups were identified among those already selected for liver resection, and this information can be used in the process of decision making on liver resection for metastatic disease. Similarly, the administrative nature of the NIS database prevents it from capturing and adjusting for important perioperative clinical factors, and thus limits the ability to examine other important factors, such as the distribution of liver metastases, the number of segments resected and the development of postoperative complications. In addition, as the NIS includes information on individual hospital stays only, it lacks information on treatments received prior to the hospital stay, such as chemotherapy, as well as follow-up data, such as 60-day postoperative mortality and longterm survival. However, the goal of the study was to examine the association of age with mortality and need for transitional care on a broader scale; the utilization of a population-level analysis with a large sample, although limited by less detailed information, strengthens the validity of the associations found in this study and makes them more generalizable to different practices. Prospective collaborative studies and the use of systematic approaches to review published data will further enhance the ability to use more detailed information and improve the selection process when elderly patients with metastatic disease are considered for liver resection.

In conclusion, this study demonstrates that liver resection in well-selected elderly patients with metastatic disease is safe and associated with a low risk for mortality, even in patients within the oldest segment of the population (aged ≥75 years). The number and degree of comorbidities are the most important indicators of risk for mortality and should be assessed thoroughly when elderly patients are considered for liver resection. The risk for mortality should not cause liver resection to be withheld from elderly patients on the grounds of age alone because appropriately selected elderly patients can be expected to achieve good outcomes following hepatectomy. Conversely, elderly patients in general (aged ≥65 years) are more likely to require transitional care following hepatectomy for metastatic disease. Based on these findings, although hepatic resection can be considered to be safe in well-selected elderly patients, nearly one in five elderly patients are unable to regain their preoperative level of independence. Patients should be counselled in this regard and efforts to anticipate transitional care needs must be incorporated into the treatment pathway. Future studies should focus on establishing standardized approaches for selecting elderly patients who are likely to benefit from liver resection with regard to both postoperative outcomes (i.e. mortality) and patient-centred outcomes (including the recovery of premorbid health and subsequent quality of life), and on incorporating these outcomes into the decision-making process when liver resection in an elderly patient is considered.

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Conflicts of interest

None declared.

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