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Liver resection in octogenarians

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Abstract

Background. Liver resections are increasingly being performed safely in elderly patients. There are no present reports of the operative safety in elderly patients. There are no present reports of the operative safety of liver resection in octogenarians who represents rapidly increasing segment of the population. The purpose of this study was to analyse the results of liver resection in octogenarians over a 5 year period within a tertiary referral liver surgery unit. *Methods*. Prospective data collection and analysis of octogenarians having liver resection between 1999 and 2004. Retrospective detailed case note analysis was performed to determine peri-operative mortality and morbidity. Comparison were made to other large series of liver resection in younger patient cohorts. The primary outcome measures was 30 day mortality and secondarily a detailed analysis of post-operative complications was performed. *Results*. A total of 15 octogenarians (median age 82) were identified from the database. There was 1 peri-operative mortality. The remaining patients were all alive at 1, 3 and 6 month follow-ups with a median follow-up of 18 months, The commonest indication for liver resection was metastatic colorectal cancer (n=11). The median operating time was 142.5 minutes and 67% of patients (n=10) had portal clamping for a median of 21.5 minutes. The median length of hospitalization was 12 days with an ICU stay of 1 day. 27% (n=4) had major surgical complications. A further 20% (n=3) had exacerbations of pre-existing comorbities. *Conclusion*. Liver resection can be performed safely in octogenarians within a tertiary referral unit. It has a low mortality and an acceptable level of morbidity in carefully selected octogenarians.

Key Words: *Liver, Hepatic, Resections, Safety, Octogenarians, Elderly*

Introduction

Western societies increasingly have to cope with the medical demands of a rapidly aging population. According to the Australian Bureau of Statistics, more than 580 000 Australians were above the age of 80 in the census of 2001. By the year 2011, this would increase to more than 800 000, or roughly 4% of the entire population [1]. The statistics of ageing are mirrored in other equivalent Western societies in Europe and North America. Epidemiological studies also highlight a corresponding increase in the presence of treatable malignancies in this population [2,3]. Malignancies represent the leading cause of death in Western societies [4,5].

Liver resections are the treatment of choice for a range of primary and secondary hepatic diseases [6]. Advances in surgical techniques involved in liver resections, together with improved anaesthesia and intensive care, have resulted in an impressive reduction of mortality and morbidity associated with liver resections ranging from around 20% in the 1970s to the currently achieved rates of $<5\%$ [7,8]. This has permitted a concurrent broadening of the indications for curative or palliative liver resections.

Several previous studies have demonstrated the safety of liver resections in elderly patients, mainly concentrating on patients greater than 60 years of age or septuagenarians with adequate hepatic reserve [9,10]. Our paper attempts to take this knowledge one step further and apply it to liver resections in octogenarians, an area which has not previously to our knowledge been published.

Patients and methods

A search of a prospectively created database of patients who underwent liver resections performed at the Liver Unit at St George Hospital between 1999 and 2004 revealed a total of 15 octogenarians out of a total of 820 patients. The St George Hospital is a tertiary teaching and referral hospital with a large liver surgery unit. All liver resections were performed by the senior author (D.L.M.) assisted by supervised resident surgeons in various stages in training.

Advanced age was not considered to be an exclusion criterion for liver resections. All patients eligible for liver resections underwent thorough preoperative medical and anaesthetic assessments. In order to

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assess operability and presence of extrahepatic disease, all patients had an angio-CT scan of the liver, chest CT scan, nuclear bone scan and, since 2002, PET scans. Blood samples were analysed for the presence of anaemia, renal function and liver function. All octogenarians had echocardiograms to assess left ventricular function and where appropriate based on clinical assessment, further investigations such as cardiac nuclear perfusion scanning were performed on each patient for assessment of ischaemic heart disease. Adjunctive investigations of the respiratory system with formal respiratory function tests were also undertaken in patients with pre-existing airways disease to determine operative safety.

We do not have data on how many patients were turned down for surgery or how many patients were not referred to our unit by general practitioners and oncologists because of advanced age.

Surgical palpation and intraoperative ultrasound guidance were used to ascertain the number of lesions, to determine appropriate treatment for each, whether resection or thermal ablation was more appropriate, and to determine localization with respect to the portal sheath. Parenchymal transection was performed with an ultrasonic surgical aspirator and progressive haemostasis was obtained by clips and ligation as well as argon beam photocoagulation. A case by case approach was taken for portal clamping (Pringle's manoeuvre) and when performed the clamp time was documented. All patients had a suction drain placed in the subhepatic area at the end of the operation. The presence of localized extrahepatic disease discovered during laparotomy was not a contraindication to liver resection and when present and locally resectable such an additional procedure was undertaken. Additional procedures performed on all patients included an open cholecystectomy when the gallbladder was present and for patients with colorectal metastasis a hepatic artery catheter was placed in the gastroduodenal artery for adjuvant postoperative chemotherapy if there was more than one liver lesion.

The total duration of the operation, amount of blood products transfused and any extraordinary anaesthetic events were also documented.

All patients left the operating theatre intubated and ventilated and were then treated postoperatively within an intensive care unit and transferred to a normal ward when stable. All patients were followed up after discharge at 1 month, 3 months and 6 months.

The primary outcome measure of this study is perioperative 30-day mortality and secondarily an analysis was performed of the complications after liver resections pertaining to both direct operative complications and exacerbations of pre-existing medical comorbidities. Major complications were divided into medical and surgical groups. As highlighted in the tables, major medical complications included myocardial infarction, hepatic failure, respiratory failure due to infection, pulmonary oedema or effusions and renal failure. Major surgical complications were defined as postoperative haemorrhage requiring transfusion, intra-abdominal collections and bile leaks. For the purposes of this study, liver resections included extended hepatectomies, lobectomies, single or multiple segmentectomies or subsegmentectomies.

Results

A total of 15 octogenarians underwent liver resections during the 5 years of the study. Two patients underwent repeat liver resections, both times as octogenarians. The median age of the patients was 82 (range 80–86 years) and there were nine males and six females. There were two extended right hepatectomies, two right hepatectomies, two left hepatectomies, three right posterior sectionectomies, two left lateral sectionectomies and four segmentectomies.

The most common indication for liver resection was metastatic colorectal cancer, i.e. 11 of 15 (73%). The other patients underwent liver resections for reasons such as cholangiocarcinoma ($n=2$), hepatocellular carcinoma ($n=1$) and invasive sarcoma ($n=1$). There were no patients who underwent liver resections for benign conditions.

Operative details known from previous published series to have an impact on the outcomes of liver resections are highlighted in Table I [6,11]. The median operating time was 142.5 min and selective portal ischaemia (Pringle's manoeuvre) was utilized in 10 patients (67%) for a median duration of 21.5 min. Our patients had a median length of hospitalization of 12 days and all were admitted to the intensive care unit for a median of 1 day. Seven (47%) patients required intraoperative transfusion of blood products in the form of packed red cells or fresh frozen plasma. It is also noteworthy that seven patients underwent adjunctive thermal ablation either in the form of cryotherapy or radiofrequency ablation. These procedures were usually performed in the form of edge cryotherapy or ablation of small lesions <1 cm

Table I. Operative and perioperative results.

Variable	Value
Postoperative hospitalization (days): median (range)	12 (5–33)
Operative duration (min): median (range)	142.5 (90–420)
Selective portal ischaemia (no. of patients)	10
Duration of portal ischaemia (min): median (range)	21.5 (7–50)
Intraoperative transfusions (no. of patients)	7
Median PRBC (units)	2
Median FFP (units)	4
Thermal ablation (no. of patients)	7

PRBC, packed red blood cells; FFP, fresh frozen plasma.

located away from the site of resection or in a contralateral lobe.

Table II summarizes the concomitant medical diseases present in these elderly patients who underwent the resections. The collective disease burden was unsurprisingly highest in cardiovascular diseases (87%) closely followed by respiratory diseases and metabolic diseases, as well as a range of other diseases such Parkinson's disease or other degenerative neurological diseases and also age-associated rheumatological conditions not known to have a bearing on the natural history of liver resections.

Table III highlights an analysis of complications of liver resections as analysed by the classification of Clavien [12]. Nine patients (60%) had complications but when further analysed seven patients (47%) had major medical or surgical complications according to our definition (Clavien grade 3). However, a deeper analysis revealed that only four (27%) of the aforementioned seven patient complications were surgical, with the remainder being exacerbations of concurrent medical comorbidities. When complications did occur, a trend was present of multiple organ complications occurring in a single patient with multi-organ concomitant disease. Minor complications (Clavien grade 1 and 2) included line infections, urinary tract infections, wound infections and pleural effusions that were not drained. There were no Clavien grade 4 complications.

At the end of the 30-day perioperative period, one patient in the series died as a result of an embolic cerebrovascular event. The remaining 14 patients were all alive at the 1-, 3- and 6-month follow-up period. The median follow-up duration was 18 months and the range was 12–48 months.

Table II. Concomitant diseases in octogenarians undergoing liver resections.

Concomitant disease	*n* (total = 15)
Cardiovascular	
Hypertension	9
Hypercholesterolaemia	9
Myocardial infarction/unstable angina	4
Arrhythmia	4
Thromboembolic disease	1
Stroke/TIA	4
Congestive cardiac failure	4
Peripheral arterial disease	4
Respiratory	
Asthma	1
Chronic airways disease	4
Metabolic	
Diabetes	3
Osteoporosis/metabolic bone disease	4
Thyroid disease	0
ASA status	
2	7
3	7
4	1

TIA, transient ischaemic attack.

Table III. Complications of liver resections.

Complications	*n* (total = 15)
Major surgical complications	
Haemorrhage	1
Intra-abdominal collections	4
Bile leak	1
Pleural effusion requiring drainage	3
Sepsis	3
Major medical complications	
Myocardial infarction	1
Cardiac failure	2
Hepatic failure	0
Respiratory failure (pneumonia or airways disease)	3
Renal failure	0
Total nil complications	6
Total major complications	7
Total minor complications only	2

Discussion

Developed countries are witnessing an increasing life expectancy and with the progressive greying of the population in the coming decades, there is no doubt that there will be an increasing demand for liver resections in the elderly for metastatic disease. Advances in perioperative anaesthesia and intensive care have made such an aggressive approach to liver resections feasible [13]. Most previous published studies of liver resections in elderly patients have focused exclusively on the outcomes for resections of hepatocellular carcinoma with some recent studies showing the reports of resections for colorectal carcinoma [14–16]. Others have had multiple indications for resections but all the studies have looked at patients above the age of 65 or 70. This is the only reported series of liver resections in octogenarians.

Our results indicate that although liver resection is still a high risk procedure, when performed within a specialized unit of surgeons, anaesthetists and intensivists it can be offered to wide group of patients including octogenarians. It has a low mortality and acceptable levels of morbidity when compared with other major surgical procedures. Previous studies concentrating on a relatively younger group of patients have highlighted the mortality of major liver resections exceeding 10% in elderly patients within their cohorts [4,17]. Other studies which have specifically aimed to look at the impacts of such surgery in the elderly have also corroborated the increased morbidity of hepatic surgery in elderly patients, quoting morbidity rates in the order of 30–50% [4,5,9].

The one mortality in our series was a patient who died 4 days after discharge from the high dependency unit to the general ward secondary to a cerebrovas-

cular event. This patient, who had experienced a previous stroke, was further predisposed to the event by the presence of chronic atrial fibrillation for which was he was anticoagulated with warfarin preoperatively. The anticoagulation had to be ceased perioperatively to reduce the risk of operative bleeding. Only lower dose anticoagulation for thromboembolism prophylaxis with subcutaneous heparin was recommenced postoperatively rather than a therapeutic dosage at a level comparable to what he was on previously. He was classified as an ASA 4 anaesthetic risk preoperatively but ultimately a choice was made to proceed with surgery in view of symptomatic local invasion, obstruction and bleeding to curatively resect the colorectal metastasis. As noted from our results, the remaining 14 patients were all alive at 1-, 3- and 6-month follow-ups. All these patients were functioning at or above their preoperative quality of life. This was assessed by means of patient and family feedback rather than formal quality of life assessment scale.

The major surgical morbidity in our series was postoperative intra-abdominal collections, usually located in the subphrenic or subhepatic spaces, requiring drainage and intravenous antibiotics. Postoperative sepsis and pleural effusions requiring drainage followed closely. Exacerbation of medical comorbidities accounted for the other major complications. Patients with pre-existing airways disease often developed atelectasis, three of whom progressed to florid pneumonia requiring intensive physiotherapy and intravenous antibiotics. Non-surgical complications were treated within a multi-disciplinary team involving consultations with specialist physicians. This was especially important in the context of multi-system medical complications occurring in individual patients. However, it is noteworthy that our rates of such complications are not higher than comparable published results [5,6]. As evidenced by our other results, this level of morbidity had no impact on the overall length of hospitalization. No complication required a further operation under anaesthesia. We can thus infer that when treated appropriately with an aggressive non-operative approach such complications are well tolerated by octogenarians.

During liver resections, we attempted to minimize intraoperative blood loss as well as preserve as much functioning hepatic reserve as possible. The amount of blood lost is often difficult to quantify and, using the intraoperative transfusion requirement as a surrogate marker, it can be noted that a 47% transfusion requirement with a median two units of packed red cells is in line with other large series on younger patient cohorts [5,9]. A reduction in perioperative blood loss is one factor that has been shown in other cohorts to be responsible for a drop in mortality and morbidity after hepatic resections [6,7,11]. The extent of transfusion was closely correlated with the duration of operations ($p < 0.01$) rather than the extent of resections as defined by number of hepatic segments, especially when operative time exceeded 120 min. We paid a significant amount of attention to meticulous approach to minimizing blood loss in our patients and our morbidity and mortality rates reflect such an approach.

As far as the operations are concerned, our usage of selective portal ischaemia, median duration of Pringle's manoeuvre as well as median operative duration are comparable to other series reporting similar procedures on younger patient cohorts [5,6,9]. This demonstrates the important fact that these variables are more related to a combination of good surgical technique and a healthily functioning hepatic parenchyma that is uninvolved with disease than to the age of the patient per se.

We discharged our patients at a median duration of 12 days when they were pain-free, mobilizing adequately at pre-morbid levels, tolerating a normal oral food intake and felt psychosocially capable of managing at their usual domicile.

In our series, no single factor was found to be independently predictive of morbidity and mortality.

Our results would indicate that if liver resections are performed in carefully selected octogenarian patients with preoperative optimization of organ system functions, as well as postoperative management within an intensive care unit, the results can match those achieved by younger patient cohorts. This is achieved within our unit by prior assessment at the pre-admission anaesthesia clinic where a multi-speciality approach is taken for the management of medical comorbidities. Special attention is given to investigation of the cardiovascular and respiratory systems and consultations with specialty physicians are undertaken. It is our opinion that liver resections should not be undertaken without full investigations and optimization of medical comorbidities if excellent results are to be obtained from anaesthesia, surgery and postoperative care. This includes, for example, performing interventional cardiovascular coronary revascularization in patients with significant ischaemic heart disease. If such optimization of physiological function is undertaken, we are of the opinion that there are no limits to the extent of resections based on age.

The survival benefit from liver resections for malignancy in octogenarians is an important issue that we did not intend to address in this study, as a significant number of patients in our series are still within their 6 months to 1 year follow-up period. However, we do know that metastatic colorectal cancer is associated with an increase in median survival from 4–6 months in untreated patients to about 9–12 months in patients treated with chemotherapy alone [18]. When colorectal metastasis is present and resected and adjuvant chemotherapy is given, the survival can be up to 40% at 5 years [19]. We are also aware of studies highlighting similar

3- and 5-year survival figures in elderly patients compared to younger patients when complete tumour resection is obtained [20,21]. Such figures may be mirrored in otherwise healthy octogenarians. Nonetheless, the effects of major concomitant disease when present may independently cause morbidity and mortality which may raise doubts about the potential benefits of cancer surgery in such elderly patients. Hence it is important to once again emphasize the importance of appropriate patient selection for this procedure.

The societal value of cancer surgery in old people and whether the cost is 'worth it' is clearly an important issue which we did not intend to address, but from the patient's viewpoint when they are carefully selected in an experienced unit, they can be offered very similar results to younger patients. Furthermore, as our theatre time and hospitalization duration are similar, presumably so are the costs.

Conclusion

Our results would indicate that liver resections in octogenarians can be performed with low levels of mortality and morbidity. The operative analysis and postoperative recovery course are comparable to those in younger patients. Certainly in metastatic colorectal cancer, where longer-term survival data are encouraging, a curative resection should be offered to patients who are fit for a general anaesthetic. A longer follow-up period of analysis is required to determine the impact of recurrence and mortality from concomitant disease in octogenarians.

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