

Resection of biliary mucinous cystic neoplasms of the liver: a prospective cohort series of 13 consecutive patients

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Background: Biliary mucinous cystic neoplasms (BMCNs) are uncommon neoplastic septated intrahepatic cysts which are often incorrectly diagnosed and have the potential for malignant transformation.

Objectives: To assess the outcome of surgical resection of BMCNs.

Methods: A prospective liver surgery database was used to identify patients who underwent surgery at Groote Schuur Hospital Complex for BMCN from 1999 to 2015. Demographic variables including age and gender were documented as well as detailed preoperative imaging, location and size, operative treatment, extent of resection, histology, postoperative complications and outcome.

Results: Thirteen female patients (median age 45 years) had surgery. Eleven were diagnosed by imaging for symptoms. Two were jaundiced. One cyst was found during an elective cholecystectomy. Five cysts were located centrally in the liver. Before referral three cysts were treated with percutaneous drainage and two were treated with operative deroofing. Six patients had anatomical liver resections and seven patients had non anatomical liver resections of which two needed ablation of residual cyst wall. One patient needed a biliary-enteric reconstruction to treat a fistula. Median operative time was 183 minutes (range: 130–375). No invasive carcinoma was found. There was no operative mortality. One surgical site infection and one intra-abdominal collection were treated. Two patients developed recurrent BMCN after 24 months.

Conclusion: BMCNs should be considered in middle aged women who have well encapsulated multilocular liver cysts. Treatment of large central BMCNs adjacent to vascular and biliary structures may require technically complex liver resections and are best managed in a specialised hepato-pancreatico-biliary unit.

Key words: Biliary mucinous cystic neoplasm, biliary cystadenoma, liver cysts, benign liver tumours

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Introduction

Biliary mucinous cystic neoplasms (BMCNs) are uncommon multilocular hepatic cysts which account for less than 5% of liver cysts.¹ BMCNs are often incorrectly diagnosed and have the potential for malignant transformation.² Clear guidelines are scant and publications are limited to small case series of BMCNs.^{3,4} Most occur in middle-aged women. Patients may be asymptomatic and the tumours are often discovered incidentally during imaging or at laparotomy. Management is complicated because accurate identification of the invasive form before surgery is seldom possible. The potential for malignant transformation and the tendency to recur, particularly when treated with techniques other than complete excision, are of concern in these tumours. In this study we describe the surgical treatment of 13 patients with BMCNs from a single tertiary centre.

Materials and Methods

A retrospective analysis of a prospectively maintained database of all liver surgery at Groote Schuur and the University of Cape Town Private Academic Hospitals between 1999 and 2015 was performed to identify all patients with a histological confirmed BMCN, based on the WHO diagnostic criteria.⁵ Patient demographics, clinical presentation and detailed preoperative imaging characteristics of the tumour, including intrahepatic location were recorded. The extent of the surgical procedure was detailed and included operative time and blood transfusion requirements. Postoperative complications were documented according to the Clavien-Dindo (CD) classification.⁶ Patients were planned for routine six-monthly follow-up. Initial surveillance investigation was abdominal ultrasound and additional investigations, for example CT or MRI were performed as clinically indicated. Descriptive analyses were used to characterise the study

population. The registry for liver resections (R024/2014) and the analysis of this subgroup (735/2016) were approved by the Faculty of Health Sciences Human Research Ethics Committee of the University of Cape Town.

Results

During the study period 457 liver resections were performed of which 13 were for BMCN. All 13 were females with a median age of 45 years (range 22–74). The clinical characteristics are summarised in Table 1. Ten patients presented with abdominal pain, eight had a palpable mass and two were jaundiced. In 12 patients the presumptive diagnosis was made on preoperative imaging (CT = 11, US = 1) while one cyst was found incidentally during an elective laparoscopic cholecystectomy (Figure 1). Median cyst size was 13 cm (range 2.5–30 cm) and most occurred centrally in the liver, abutting the hilar bilio-vascular structures. Three patients had percutaneous aspiration of cysts before referral. In two patients inappropriate deroofing was performed before referral. In one, treated as a simple cyst, histology confirmed a BMCN, while in the other a persistent bile leak after deroofing required a formal liver resection.

The operative technique and procedure were adapted to the cyst size and location and proximity of the cyst to vital structures in the porta hepatis, the hepatic veins and the inferior vena cava (Table 2) (Figure 2). In two patients in whom the back wall of the BMCN was adherent to major vascular structures, as much of the cyst wall as could be safely resected was removed and the residual inner cyst surface was ablated with argon beam coagulation. In one patient with a complex centrally located cyst in whom the left hepatic duct communicated with the cyst cavity, a biliary-enteric reconstruction with a Roux-en-Y loop was performed. Four patients had bile leaks identified during surgery that were oversewn. Two patients had postoperative complications. In one patient a CD grade II surgical site infection was

successfully treated with antibiotics and in the other a grade IIIa intra-abdominal collection required radiological percutaneous drainage one month after surgery. Four patients had frozen section performed on the cyst wall intraoperatively, all confirming mucinous neoplasms. None of the patients had invasive BMCN on histology (Figure 3).

All patients had a follow-up after surgery, but long term follow-up, more than 1 month, was only possible in 7 patients with a median follow-up of 12 months (range 1–24 months). Two patients developed recurrent disease after 24 months. Both recurrences were diagnosed on CT scan after new symptoms were investigated. One recurred after partial resection with ablation of the remnant cyst wall and declined further surgery. The other who recurred after a formal resection was treated with percutaneous aspiration and ethanol injection because of a high operative risk. She remains recurrence-free after eight years.



Figure 1. CT axial image of patient 8 demonstrated a typical central placed complex liver cyst

Table 1. Clinical characteristics of patients

Patient	Age	Symptoms	Clinical Signs	Maximum diameter (cm)	Location (segments)
1	46	RUQ pain	Jaundice & epigastric mass	15	Central (4,5)
2	47	N&V, LOW	Palpable epigastric mass	25	Right (5,6)
3	39	RUQ pain	None	2,5	Right (5)
4	48	Epigastric discomfort	Palpable epigastric mass	NA	Central (2,3,4,5)
5	74	Epigastric discomfort	None	NA	Left (2,3)
6	22	RUQ pain	Jaundice & epigastric mass	12	Central (4,5)
7	32	Biliary colic	None	10	Left (3)
8	45	Abdominal distention	Palpable epigastric mass	21	Central (4,5,6)
9	35	RUQ pain	Previous surgery	8	NA
10	56	RUQ pain	Palpable epigastric mass	10	Right (5)
11	44	Epigastric discomfort	NA	NA	Right(5,6)
12	38	Abdominal distention	Palpable epigastric mass	30	Central (4,5,8)
13	63	Epigastric discomfort	Palpable epigastric mass	14	Left (2,3)

RUQ right upper quadrant; N&V nausea and vomiting; LOW loss of weight; NA not available

Table 2. Operative procedures (n = 13)

Operation	
Anatomical liver resection	6
Non-anatomical liver resection	
Complete	5
Incomplete resection with ablation	2
Inflow occlusion	2
Intra-operative blood transfusion	1
Intra-operative frozen section performed	4
Drain	11
Operative time (minutes), median (range)	183 (130-375)
ICU stay (days), median (range)	2 (1-3)
Hospital stay (days), median (range)	7 (5-8)

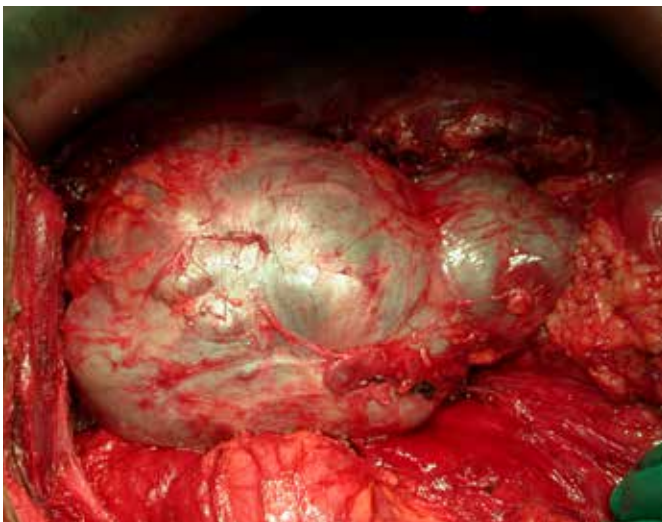


Figure 2. Exposure of BMCN before resection

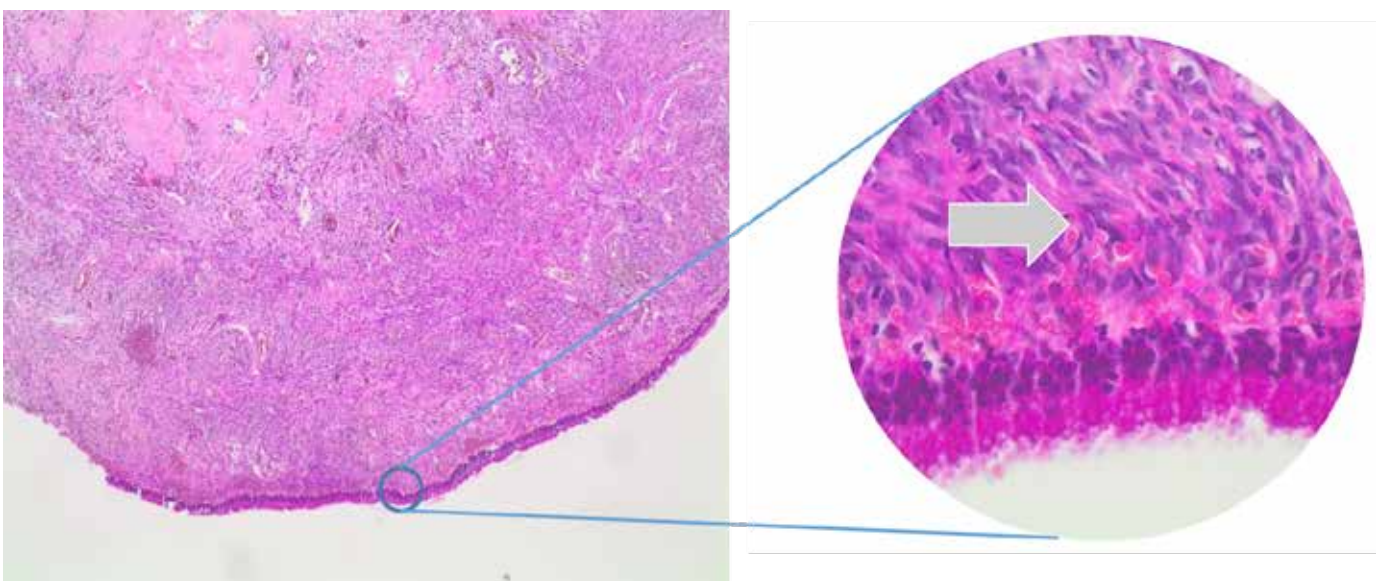


Figure 3. Low and high power histology slides of a BMCN wall with the arrow indicating the ovarian-like stroma

Discussion

In this study all patients were females with a median age of 45 years which is in keeping with the literature that reports a female BMCN preponderance of 90%, typically in the fourth and fifth decades of life.^{1,7} The majority of patients presented with cyst-related symptoms as summarised in Table 1. Some BMCNs in our series were mistaken for simple cysts which led to inappropriate initial treatment, including aspiration and deroofting. Patients with incomplete initial resection develop recurrent symptoms and are at risk for malignant transformation, and thus require definitive surgery for complete resection.^{2,8} Older age, male gender and shorter duration of symptoms on presentation are associated with a greater risk of invasive BMCN.⁹

Abdominal ultrasound typically shows well-demarcated, mostly multilocular hyperechogenic cystic lesions, which may show septae and characteristic papillary projections from the cyst wall.¹⁰ As in our patients, common features on CT include low-density, well defined, lobulated, multilocular, thick-walled cystic lesions with internal septa and occasionally mural nodules.^{5,10} CT also provides additional information regarding the anatomic relation of cysts to major vessels and bile ducts as well as surrounding structures. MRI/MRCP may be of value in assessing proximity to the intrahepatic biliary system and possible biliary communication of cysts, which would make BMCNs unlikely.¹¹ By and large, a CT scan will suffice as imaging modality and MRI is unlikely to change management. In most of our patients the typical imaging findings of a large, solitary multiloculated complex liver cyst with internal septation and nodularity was present. Most cysts occurred centrally in the liver, straddling right and left lobes and in close relation to the porta hepatis.

Serum markers were found not to be helpful in the diagnosis in this series, which is in keeping with the results of Wang et al. who in a series of 30 patients found that CA19.9 to be

elevated in only 17 patients.¹² CA19.9 was available in four of our patients with only one being elevated. Fine needle aspiration with cyst fluid analysis was not used in this current study because of potential harm in disseminating malignant cells and has not proven to change the management plan.¹¹

As in our study only a minority of patients present with complications such as jaundice, cyst rupture, bacterial infection or intracystic haemorrhage. Rare complications such as biliary fistulae and inferior vena cava obstruction have been described.⁴ Although all the patients in this study had benign features on histology, malignant change has been reported in up to 10% of patients.¹³

The only appropriate surgical strategy for treatment of BMCNs is complete resection with negative margins, either as anatomical or non-anatomical liver resection, depending on the position of the cyst and the relationship to vital structures. The complexity of management is illustrated in a global multi-centre analysis of 248 patients in which 10% of patients had malignant transformation to invasive BMCNs and 18.3% recurred after inadequate surgery.¹³ In the largest single-centre cohort of 39 patients, seven were misdiagnosed before initial surgery. Liver resection was performed in 17 patients (eight right and nine left hemi-hepatectomies) and enucleation was performed in 22 patients. At a median follow-up of 20 months, one patient presented with recurrence.³ In our series, six patients had anatomical resections and seven had non-anatomical resections, while two of these needed ablation of residual cyst wall (Table 2). Alternative techniques such as aspiration, internal drainage, intratumoral sclerosant application and incomplete resection result in recurrence rates of 90–100%. Intraoperative frozen section of the cyst wall has not been shown to alter the operative procedure as the biopsy could be non-representative.¹⁴ There is a single case report of a liver transplant for a central symptomatic BMCN involving the main vasculobiliary structures.¹⁵

As in our series, the short-term operative morbidity in published series is low and the prognosis in completely resected BMCNs is excellent.^{1,12,16} Even though recurrence after an adequately treated cyst is less than five percent, follow-up with abdominal ultrasound after resection is recommended.

Conclusion

BMCNs should be considered in middle-aged women who have well encapsulated multilocular liver cysts. Assessment and treatment of all BMCNs should be in a specialised hepatopancreatico-biliary unit in view of their malignant potential and propensity to recur after resection. Treatment of large central BMCNs adjacent to vascular and biliary structures in particular may require technically complex and challenging liver resections.

Conflicts of interest

The authors declare no conflict of interest.

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