Size of common bile duct stones on MRCP predicts likelihood of positive findings at ERCP

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Abstract

Objective:

To ascertain if direct measurement of the size of common bile duct stones (CBD) on magnetic resonance cholangio-pancreatography (MRCP) can be used to predict the likelihood of a positive endoscopic retrograde cholangio-pancreatography (ERCP) result. Should we be carrying out ERCPs on all patients with CBD stones?

Methods:

We retrospectively analysed the records of 1812 consecutive patients undergoing MRCP between November 2009 and November 2014 at the Victoria Infirmary. A measurable CBD stone was present in 383 patients, of whom 293 successfully underwent ERCP.

Results:

221 patients (75%) had stones demonstrated on ERCP. A receiver operating curve (ROC) was plotted correlating stone size with the likelihood of a positive ERCP result, and demonstrates that using a cut off of >4 mm as an indication for ERCP gives the mathe- matical best-fit correlation with a sensitivity of 83% (95% CI 78,88) and specificity of 66% (95% CI 53,77).

Conclusions:

In our current practice, all patients with CBD stones at MRCP are considered for ERCP regardless of stone size. Our results would support the hypothesis that as size de- creases the likelihood of spontaneous stone passage increases. Although the threshold of mathematical best compromise is >4 mm to minimise both type 1 and type 2 errors, we would favour a lower threshold of 2 mm above which ERCP is performed (sensitivity 98.65, 95% CI 96.1,99.7, specificity 25.71%, CI 16.0,37.6). For patients with stones measuring 2mm or less, early operative intervention with intraoperative cholangiography to confirm duct clearance could be a suitable alternative.

Introduction

Gallstones are present in approximately 25% of the UK population at post-mortem,[1] and complications including common bile duct (CBD) stones account for a significant part of emergency and elective general surgery.[1,2] The current guidelines issued by the British Society of Gastroenterologists suggest that whenever patients have symptomatic CBD the stones should be removed whenever possible.[3] They also state that a cholecystectomy should be performed for all patients with CBD stones when accompanied by symptomatic gallstones.[1,3]

The standard sequence of investigation for suspected CBD stones involves transabdominal ultrasound to assess CBD size and plasma liver function tests in the first instance. If either of these is abnormal the next step would be to carry out an MRCP or endoscopic ultrasound.[4] Both of these tests have a higher sensitivity for the identification of gallstones particularly CBD stones.[4-6] If stones are confirmed, the current guidelines state that endoscopic retrograde cholangio-pancreatography (ERCP) and stone extraction should be performed on all patients fit to undergo the procedure.[3]

ERCP carries significant risks to the patient, with a reported rate of post ERCP pancreatitis as high as 6.7%, gastro-intestinal haemorrhage of between 0.7% and 2%, cholangitis between 0.5% and 5% and duodenal perforation up to 1%.[1,6,7] Current guidelines state that patient selection should take into ac- count patient co-morbidities and the likelihood of a negative investigation, and caution against unnecessary biliary instrumentation, stating that ERCP should be reserved for those patients in whom the clinician is confident an intervention will be required. The Joint Advisory Group on Gastrointestinal endoscopy (JAG) recommendations state that >90% of ERCPs[8] should be performed with therapeutic intent, which is considerably higher than the rate of positive ERCP in our hospital.

In the management of ureteric stones, radiological evaluation of stone size has been shown to clearly correlate with the chance of spontaneous stone passage.[1,9] While the ureter is of a larger diameter than the CBD and the volume of urine which is a much less adhesive substance than bile is much larger over the course of 24h no similar studies looking to correlate stone size to the chance of passing have been carried out.[4,9]

As a result, we set out to investigate whether or not CBD stone size measured on MRCP could be used as a predictor of the likelihood of finding CBD stones at ERCP, and thus whether a size

threshold could be set to avoid ERCP in patients with a high risk of an unnecessary procedure.

Methods

Clinical records were reviewed over the 60 month period from November 2009 to November 2014 to identify those patients who had a clinical diagnosis of possible CBD stones at a single unit in Glasgow. The results of this review were then correlated with those patients who underwent MRCP scans to ensure that these were for gallstone disease as opposed to another cause. Stone sizes and CBD dilation were reported by a consultant radiologist or a senior registrar via the PACS imaging system.

Those patients who had confirmed MRCP stones were then reviewed to ascertain if they proceeded to ERCP. The reports for each ERCP were reviewed in order to ascertain if these were successful or not and if not the reason why this was the case.

All MRI scans were carried out using a Phillips Achieva 1.5 T MRI scanner. Data was analysed using MedCalc version 13.

All clinical information was stored in an encrypted Microsoft Excel 2007 file. This was in turn stored a secure serve in accordance with local policy in Greater Glasgow and Clyde. Statistical analysis was carried out in SPSS with graph construction also being carried out in SPSS. Statistical analysis was performed by plotting a receiver operating curve (ROC) of true positive rate (sensitivity) against false negative rate (1- specificity). From this, the sensitivities and specificities of a range of size cut-offs were derived, as well as the value of best mathematical compromise (greatest area under the curve).

Results

Over the course of the study 1812 consecutive patients with a clinical diagnosis of possible CBD stones underwent MRCP. Stones were demonstrated in 408 patients. Stone size was measured and reported by a consultant radiologist or senior Specialist Trainee Registrar in 383 patients. The remaining 26 were excluded as no measurement was given on the original MRCP report and the images were not available for re-reporting.

73 patients did not undergo ERCP. These patients declined the procedure, were clinically unfit, died prior to ERPC or were otherwise lost to follow-up. ERCP was positive in 221 (75%) patients. 17 ERCPs failed, and the remaining 72 patients were demonstrated to have a clear duct. Stone size

ranged from 1 to 32mm (median 6mm).

Figure 1 shows the ROC curve quantifying the ability of MRCP measurement of stones to predict ERCP result, with the area under the curve calculated at 0.79 (95% CI 0.74, 0.84, p<0.0001). The point of mathematical best compromise (Youden index J associated criterion) is shown as stone size >4mm.

Table 1 shows criterion values and co-ordinates of the ROC curve, which presents sensitivity and specificity for a variety of thresholds used as a cut-off to decide whether or not to perform ERCP.

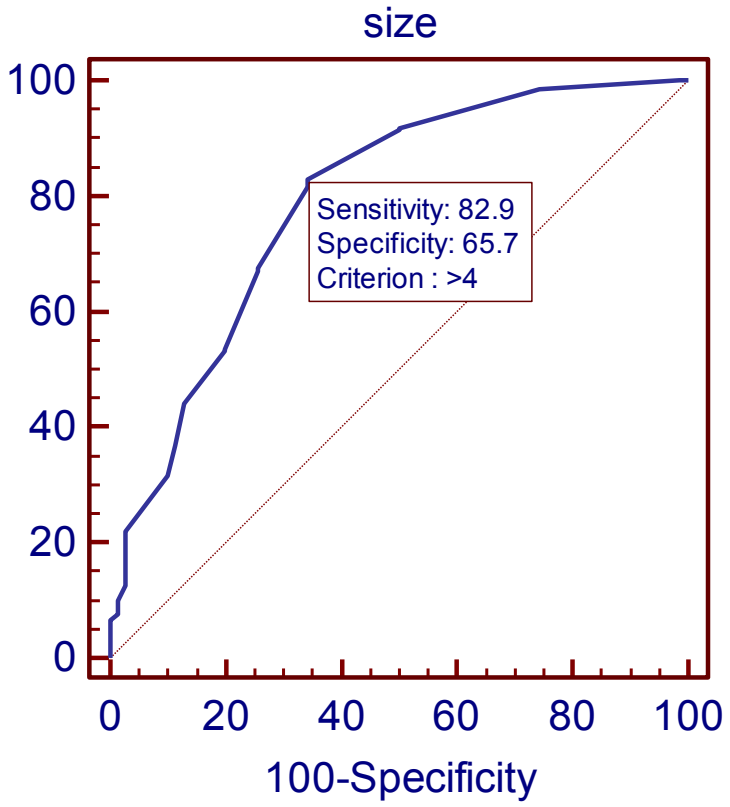

Figure 1: ROC curve showing sensitivity and specificity

Criterion	Sensitivity	95% CI	Specificity	95% CI	+LR	-LR
≥1	100.00	98.4 - 100.0	0.00	0.0 - 5.1	1.00	
>1	100.00	98.4 - 100.0	1.43	0.04 - 7.7	1.01	0.00
>2	98.65	96.1 - 99.7	25.71	16.0 - 37.6	1.33	0.053
>3	91.89	87.5 - 95.1	50.00	37.8 - 62.2	1.84	0.16
>3.5	91.44	87.0 - 94.8	50.00	37.8 - 62.2	1.83	0.17
>4	82.88	77.3 - 87.6	65.71	53.4 - 76.7	2.42	0.26

>4.5	81.53	75.8 - 86.4	65.71	53.4 - 76.7	2.38	0.28
>5	67.57	61.0 - 73.7	74.29	62.4 - 84.0	2.63	0.44
>5.5	67.12	60.5 - 73.3	74.29	62.4 - 84.0	2.61	0.44
>6	53.60	46.8 - 60.3	80.00	68.7 - 88.6	2.68	0.58
>6.2	53.15	46.4 - 59.9	80.00	68.7 - 88.6	2.66	0.59
>7	44.14	37.5 - 50.9	87.14	77.0 - 93.9	3.43	0.64
>8	36.94	30.6 - 43.7	88.57	78.7 - 94.9	3.23	0.71
>9	31.53	25.5 - 38.1	90.00	80.5 - 95.9	3.15	0.76
>10	22.07	16.8 - 28.1	97.14	90.1 - 99.7	7.73	0.80
>12	12.61	8.5 - 17.7	97.14	90.1 - 99.7	4.41	0.90
>13	9.91	6.3 - 14.6	98.57	92.3 - 100.0	6.94	0.91
>14.5	7.66	4.5 - 12.0	98.57	92.3 - 100.0	5.36	0.94
>15	6.76	3.8 - 10.9	100.00	94.9 - 100.0		0.93
>32	0.00	0.0 - 1.6	100.00	94.9 - 100.0		1.00

Table 1: Criterion values and co-ordinates of the ROC curve

Discussion

After a detailed literature review we believe that no previous studies have been published examining the relationship between size of CBD stones and their chance of spontaneous passage. Our data suggest that there is a highly significant correlation between increasing stone size and the likelihood of positive ERCP (p value < 0.0001). This strongly suggests that there is a higher likelihood of smaller stones passing spontaneously prior to attempts at removal via endoscopic means. This is not the standard practice in the majority of centres within the UK and as such we hope will generate considerable debate.

If we were to reduce the number of unnecessary ERCPs, the data would support setting a threshold of stone size, which any given stone must exceed on MRCP measurement before ERCP would be undertaken.[4] As can be seen in Table 1, as that threshold rises, the specificity of the test rises with it, at the cost of a falling sensitivity. If ERCP is performed for any stone >1mm in size, sensitivity is 100% (95% CI 98.4, 100) but with a low specificity of 1.43% (95% CI 0.04, 7.1) and correspondingly high false negative rate - in essence, this is close to our current practice of performing ERCP on all patients with MRCP demonstrated stone disease of any size.[1,4]

By contrast, if a threshold of >15 mm is set below which ERCP is not undertaken, the sensitivity of the test falls to 6.76% (95% CI 3.8, 10.9) and the specificity rises to 100% (95% CI 94.9, 100). Clearly the most useful threshold, at which a good sensitivity and specificity is maintained lies

somewhere between these two levels.

Mathematically, the point of best compromise (maximal value of Youden's index) sets a threshold of >4mm for undertaking ERCP, with a sensitivity of 82.88% (77.3, 87.6%) and specificity of 65.71% (53.4, 76.7%) which overall minimises the number of misclassified results. However, the test gives equal weight to the consequences of patients with stones being left untreated and those with a clear duct undergoing unnecessary ERCP, which is not clinically the case.[6] In practice it would seem more important to accept a lower specificity in order to gain a greater sensitivity, to avoid the consequences of under-treatment.[1] Even a relatively modest decrease overall in the number of unnecessary ERCPs performed would be an improvement on the current situation, not only reducing the clinical risk to any given patient, but also with implications for waiting lists and resource management if fewer numbers of procedures are performed overall.[10,11] From these data, we would suggest that a cut off of >2mm in stone size would result in very few stones being missed (sensitivity of 98.65, 95% CI 96.1, 99.7), while still correctly identifying a significant number of patients not requiring ERCP (sensitivity 25.71%, CI 16.0, 37.6).

Conclusions

In our current practice, all patients with CBD stones at MRCP are considered for ERCP regardless of stone size, which leads to a rate of positive ERCP falling significantly short of the JAG recommendation of 90%.[8] Our results support the hypothesis that as size decreases the likelihood of spontaneous stone passage increases, and that measurement of stone size can be used to predict the likelihood of positive ERCP. Although the threshold of mathematical best compromise is >4mm to minimise both Type 1 and Type 2 errors, we would favour a lower threshold of 2mm above which ERCP should be performed (sensitivity 98.65, 95% CI 96.1, 99.7, sensitivity 25.71%, CI 16.0, 37.6) in order to exclude a significant proportion of patients for where an ERCP is unnecessary. For patients with stones measuring 2mm or less, early laparoscopic cholecystectomy with intraoperative cholangiography to confirm duct clearance could be a suitable alternative to ERCP.[11] A randomised controlled trial is needed to establish efficacy and safety in clinical practice.

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