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Prospective evaluation of early endoscopic ultrasonography for triage in suspected choledocholithiasis: Results from a large single centre series

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ABSTRACT

Background: Endoscopic ultrasonography is accurate, safe, and cost-effective in diagnosing common bile duct stones, thus suggesting the possibility to avoid invasive endoscopic retrograde cholangiopancreatography.
Aim: To prospectively evaluate the diagnostic and therapeutic performance of early endoscopic ultrasonography in suspected choledocholithiasis.
Patients and methods: All consecutive patients presenting to the Emergency Department with suspicion of choledocholithiasis between January 2010 and January 2012 were evaluated and categorized as low, moderate, or high probability of choledocholithiasis, according to accepted criteria. Endoscopic endosonography was carried out within 48 h from the admission and endoscopic retrograde cholangiopancreatography was performed soon in case of confirmed choledocholithiasis.
Results: Overall 179 patients were included: 48 (26.8%) were classified as low, 65 (36.3%) as moderate, and 66 (36.9%) as high probability of choledocholithiasis. Of the 86 patients with common bile duct stones at endoscopic endosonography, endoscopic retrograde cholangiopancreatography confirmed the finding in 79 (92%). By multivariate analysis only the common bile duct diameter proved an independent predictor of common bile duct stones.
Conclusions: Early endoscopic endosonography is accurate in identifying choledocholithiasis allowing immediate endoscopic treatment and significant spare of unnecessary endoscopic retrograde cholangiopancreatography. This approach can be useful as a triage test to select patients not needing endoscopic retrograde cholangiopancreatography, allowing, in selected cases, their early discharge.

1. Introduction

Common bile duct stones (CBDS) represent a relatively common clinical finding: they are detected in 5–15% of patients with symptomatic cholelithiasis, 10–20% of patients undergoing cholecystectomy, and 18–21% of those with gallstone pancreatitis [1,2]. Intraductal stones carry a clear risk for abdominal pain, pancreatitis, ascending cholangitis, and partial or complete biliary obstruction, in turn responsible for extrahepatic cholestasis, cholangitis, hepatic abscesses, or pancreatitis [3]. Accordingly, when present, their removal is strongly recommended. However, CBDS diagnosis can be difficult due to the lack of specificity of both clinical and biochemical findings.

At present, when dealing with CBDS, standard non-invasive imaging modalities, including transabdominal US and CT, show a sensitivity of 25–58% and a specificity of 68–91% [4]. According to clinical biochemical and radiological tests [4], patients with suspected CBDS can generally be categorized according to their low (<10%), intermediate (10–50%), or high (>50%) probability to develop the condition, and a number of different prognostic scores have been proposed to predict the presence of CBDS [5–11]. The recently published ASGE guidelines, which focus on the role of endoscopy in the evaluation of suspected CBDS, suggest – for patients with symptomatic cholelithiasis – a management algorithm based on the degree of probability of having CBDS [12]. However, to date, the reliability of the commonly used

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biochemical and radiological findings in CBDS prediction has already been firmly challenged [13]. Starting about 10 years ago, different studies have shown that the endoscopic retrograde cholangiopancreatography (ERCP)-guided approach may be more cost saving, as most patients would then require ERCP anyway [14–16]. However, Buscarini et al. [17] found CBDS in 66.4% and 44.2% patients at high and intermediate risk of biliary obstruction, respectively. Besides, large prospective case series found an overall complication rate of 5–10%, and a 0.2–0.5% mortality rate after diagnostic and therapeutic ERCP [18–20]. Accordingly, the best way to minimize the risk of ERCP complications is the preferential use of ERCP for therapy rather than diagnosis. In the field considered, endoscopic ultrasound (EUS) has consistently shown to be accurate, safe, and cost effective, compared with MRCP and ERCP, in diagnosing obstructive biliary disease, thus preventing unnecessary ERCP and its related complications [21]. Moreover, 3 randomised series have clearly demonstrated that a EUS-first strategy followed by selective therapeutic ERCP can reduce diagnostic ERCP by 60–75% in patients at moderate risk for CBDS [22–24]. Based on the currently available data, the issue of whether the EUS-first strategy should be applied to all the patients with suspected CBDS instead of being limited to those at moderate risk for CBDS remains to be elucidated.

Accordingly, the present single-centre prospective pilot study was primarily aimed at investigating the clinical impact of early EUS in the management of suspected acute obstructive biliary disease caused by CBDS. Secondarily, the present study aimed at reassessing the role of endoscopy in both the evaluation and management of suspected CBDS, in contrast to the current guidelines still based on clinical and biochemical criteria.

2. Methods

This prospective study was carried out at the Gastroenterology and Endoscopy Department of a secondary referral University Hospital in north-western Italy, with an annual case load of EUS and ERCP of about 600 and 350, respectively. The study complies with the ethical guidelines of the 1975 Declaration of Helsinki and was approved by the Institutional Review Board of the Ospedale Maggiore della Carità, Novara, Italy. Written informed consent was obtained from all the patients enrolled.

All consecutive patients attending the Emergency department between January 2010 and January 2012 due to acute abdominal pain in the right hypochondrium and showing biochemical and/or radiological findings consistent with possible CBDS were prospectively enrolled after being classified at low, moderate, or high probability of CBDS, according to the risk stratification reported by Barkun et al. [5], as previously suggested by Tse et al. [4]. Exclusion criteria were: refusal to participate in the study, inability to give informed consent, unsuitability for endoscopy, presence of isolated intra-hepatic ductal dilatation, previous history of gastrectomy, previous history of sphincterotomy, ongoing acute cholecystitis (defined as increased wall thickness at ultrasound [US], altered morphology as double-track, vascular spot at colour Doppler, or the presence of pericholecystic fluid), cholangitis and/or pancreatitis, or previous clear-cut identification of a disorder responsible for biliary obstruction at US or CT. Prior cholecystectomy was not among the exclusion criteria. The exclusion of patients with acute cholecystitis and biliary acute pancreatitis was set to evaluate a more homogeneous group of patients. Moreover, patients with acute biliary pancreatitis are already considered at moderate and high probability of CBDS and, as such, represent a particular subset of patients that can be evaluated in a different study. All participants fulfilling the inclusion criteria underwent EUS within 48 h from their admission. CBDS were diagnosed in the presence of a reproducible hyperechoic focus with an associated acoustic shadowing, while the lack of associated acoustic shadowing within the extrahepatic bile duct was considered consistent with biliary sludge [25]. Number and size of all stones detected were recorded. ERCP was performed immediately after EUS only in those cases with proven CBDS or sludge.

Patients with a definite diagnosis of cholelithiasis underwent laparoscopic or open cholecystectomy within 4 weeks from their hospital discharge. Patient follow-up included a telephone call at 1, 3, and 6 months after EUS and ERCP.

2.1. Procedures

All the EUS procedures were performed by 2 expert endosonographers with more than 5 years of experience in the procedure (A.A. and M.B.). The procedures were performed by means of a linear (GF-UCT140, Olympus Optical Co., Ltd, Tokyo, Japan) or radial (GF-UM160, Olympus Optical Co., Ltd, Tokyo, Japan) scanning echoendoscope using all frequencies (i.e. 5, 6, 7.5, and 10 MHz), but mainly 7.5 MHz and 10 MHz to exclude common bile duct (CBD) microlithiasis. The two endosonographers had large experience of both radial (ca. 100 examinations/year/endosonographer) and linear probes (ca. 100 examinations/year/endosonographer). The choice of which probe to use depended on the availability at the moment of patient examination. In case of CBDS detection, therapeutic ERCP with endoscopic sphincterotomy and stone extraction was performed during the same endoscopic session under the same sedation by 2 independent investigators (A.A. and M.O.) with either 10 or 15 years of experience in the procedure. After sedation by i.v. injection of midazolam (1–2 mg) and fentanyl (50–100 gamma) the EUS transducer was inserted up to the second duodenal portion and gradually withdrawn to visualize the main duodenal papilla, extrahepatic bile duct, cystic and hepatic ducts, and gallbladder. Cholangiography at ERCP was obtained by injecting a 50%-diluted iodinated contrast agent (Ultravist® iopromide injection), starting proximally in the duct in order to avoid pushing any small stones into the intrahepatic ducts.

2.2. Statistical analysis

Clinical data were recorded in a computerized database by a single research assistant (M.G.). Continuous data are expressed as median with their interquartile range, unless otherwise stated. Proportions are given as numbers and percentages. Differences in clinical parameters among the 3 risk groups were assessed by means of the Mann–Whitney *U* test for continuous data or the chi-squared Fisher's exact test, when appropriate for proportions. All reported p values are two-tailed. A p value < 0.05 was considered statistically significant. The following predictors were investigated: age, gender, bilirubin, AST, ALT, GGT, alkaline phosphatase, amylase, fever, and CBD dilation (defined as CBD diameter ≥ 6 mm or ≥ 8 mm in case of cholecystectomy, at US). The top normal value for CBD diameter is still controversial, but generally accepted to be between 6 and 8 mm. Conventionally, the upper limit of normality for the CBD as measured by US is considered to be 6 mm [26,27]. The possible association between EUS evidence of CBD stones and individual pre-procedure predictors was first assessed by univariate logistic regression analysis, and then by entering the variables significantly associated with CBD stones ($p < 0.05$) in a multivariate logistic regression model.

3. Results

A total of 125 patients of the 324 considered for possible enrolment were excluded because of pancreatitis ($N = 50$), previous gastrectomy ($N = 2$), previous sphincterotomy ($N = 6$), cholangitis ($N = 4$), previous US or CT-based identification of CBDS ($N = 58$),