PATIENTS WITH MORTALITY AFTER ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY

Nurten Bakan1, Gulsah Karaoren1, Senay Goksu Tomruk1, Mehmet Erdem Akçay1, Semra Yanık1, Ahmet Yıldırım1, Kamil Özdi1
1Anaesthesiology and Reanimation, Umraniye Research Hospital; 2Gastroenterology, Umraniye Research Hospital, Istanbul, Turkey

Original Research
Journal of Clinical and Analytical Medicine

DOI: 10.4328/JCAM.5001
Received: 29.03.2017
Accepted: 15.04.2017
Printed: 01.04.2017

Abstract
Aim: Endoscopic retrograde cholangiopancreatography is a high-quality but invasive procedure performed for diagnosis and treatment of biliary tract, pancreatic tract and peripancreatic region diseases. Risk factors for complications include known or unsuspected premorbid conditions, problems related to anxiety and insufficient analgesia. Material and Method: We retrospectively reviewed 1471 patients who underwent elective or emergent Endoscopic retrograde cholangiopancreatography with routine monitoring and standard sedoanalgesia protocol between 2011 and 2016. Patients who had specific (surgical) and non-specific (cardiovascular, respiratory) complications during procedure and admitted to ICU were selected. Age, gender, body mass index, ASA class, comedities, duration of procedure, drugs used, complication and therapeutic interventions were assessed in remaining patient who died in ICU. Results: 10 patients had complications during procedure and internalized at ICU. 7 of them (0.47%) had died. In mortal patients, mean Charlson Comorbiditı̈e İndexı̈ was 3.00±0.81, while mean APAC(E) score was 38.71±4.07 and mean expected mortality was 88.22±7.23. Discussion: In conclusion, one should be careful in standard monitoring and patient selection in addition to physical conditions against risk factors that may increase mortality regardless of sedation method used in Endoscopic retrograde cholangio-pancreato-ography. Using APACHE II score and CCI rather than ASA score can be more effective for prediction of mortality.

Keywords
Endoskopik Retrograd Kolanjiyopankreatografi; Sedo-Analjezi; Monitorlı̈ Anestezi Bakımı; APACHE; Mortalite

Oz
Amaq: Endoskopik retrograd kolanjiyopankreatografi safra yolları, pankre-istik yollar ve perampüller bölge hastalıkları tanı ve tedavisi için uygulanan niteliği ama invazif bir işlemidir. Komplikasyonlar için risk faktörleri bilinen ve/veya şüpheli premorbid durumlar, anksiyete ile ilişkili sorunlar ve yetersiz analjezide bulunabilir. Bu çalışmada, girişimin并发症sini ve girisimle ilişkili mortalite incelendi. Gerçekten, yześem 2011 ile 2016 yılları arasında rutin monito- rizasyon ve standart sedo-analjezi protokolü ile elektif veya acil endoskopik retrograd kolanjiyopankreatografi uygulanan 1471 hasta gıkça düşük riskli- de incelendi. Girişim sırasında spesifik (cerrahi) ve non-spesifik (kalp-damar, solunum)并发症sini ve yoğun bakım ünitelerinde ex olan hastalar- da yaş, cinsiyet, vücut kitle indeksi, ASA sınıfı, Charlson Komorbidite İndeksi, APACHE II skoru, girişim süresi, kullanılan ilaclar,并发症sini ve teröpatik并发症sini değerlendirildi. Bulgular: Girişim sırasında并发症sini ve yoğun bakım ünitelerinde ex olan 10 hastanın 7’si (0,47) ex oldu ve bu hastalardaortalama Charlson Komorbidite İndeksi skoru 3.00±0.81, APACHE II skoru 38.71±4.07 ve beklenen mortalite 88.22±7.23 idi. Tartışma: Endoskopik retrograd kolanjiyopankreatografi, sedoanesthesi ve monitorlemenin bağımsız olarak mortaliteyi artrabilecek risk faktörlerine karşı standart monito- rizasyon uygulanmalı ve hasta seçiminde dikkatli olunmalıdır. APACHE II skoru ve Charlson Komorbidite İndeksinin kullanılmasi si mortalitenin öngörülmesi açısından daha etkin olabilir.

Anahtar Kelimeler
Endoskopik Retrograd Kolanjiyopankreatografi; Sedo-Analjezi; Monitorlı̈ Anestezi Bakımı; APACHE; Mortalite

DOI: 10.4328/JCAM.5001
Received: 29.03.2017
Accepted: 15.04.2017
Printed: 01.04.2017

Corresponding Author: Gulsah Karaoren, Anaesthesiology and Reanimation, Umraniye Research Hospital, Istanbul, Turkey.
E-Mail: dirgylimaz@yahoo.com
Introduction
Endoscopic retrograde cholangiopancreatography (ERCP) is a high quality but complex procedure in the diagnosis and treatment of biliary tract, pancreatic tract, and periampullary region disorders [1]. ERCP involves combined use of X-ray and a long flexible tube, namely an endoscope. The physician can visualize the lumen of the stomach and duodenum through the endoscope and inject dye into the biliary and pancreatic ducts to enable visualization on X-ray [2].

The complication rate following ERCP varies from 5% to 10% [3]. The vast majority of such complications (>90%) are mild or moderate. Nevertheless, and it is important to classify these complications as specific or non-specific in order to prevent and reduce complications [4]. Non-specific complications include those which that could might occur during any endoscopic procedures, such as hemorrhage or perforation due to passage of the endoscope, adverse effects caused by drugs used during the procedure, cardiopulmonary events, and desaturation. Specific complications include pancreatitis, sepsis, cholangitis, and hemorrhage and perforation caused by endoscopic sphincterotomy [5].

It is essential to determine risk factors for ERCP complications, which preferentially requires selection of eligible patients (Table 1). The risks can be detected in a timely way by preoperative assessment and appropriate monitoring monitoring [3,6,7].

Material and Method
We retrospectively reviewed 1471 patients who underwent elective or emergent ERCP at a semi-prone position under pharyngeal anesthesia (lidocaine spray) with routine monitoring (including ECG, non-invasive BP, SpO2) and standard sedoanalgiesia protocol (midazolam 0.02 mg kg\(^{-1}\); fentanyl, 1 mg kg\(^{-1}\); propofol 1 mg kg\(^{-1}\)) between 2011 and 2016 after approval of the local ethics committee of Umranie Training Hospital. We identified 10 patients who developed specific (surgical) and non-specific (cardiovascular, respiratory) complications during the procedure and were admitted to the ICU. Of these, 3 patients who were discharged to the ward after treatment and follow-up in ICU were excluded. Age, gender, body mass index (BMI), ASA class, comorbidities, indication, duration of procedure, drugs used, complications, and therapeutic interventions were assessed in the remaining patients who died in the ICU.

Results
Of 10 patients with complications during the procedure, it was found that one patient died during the procedure in the at ERCP unit and 6 patients died in the ward after treatment and follow-up in ICU, while remaining the other 3 patients were discharged to the ward after treatment and follow-up in the ICU. Table 2 presents demographic characteristics, comorbidities, and procedure-related data of the patients who died.

Table 2 presents potential confounders (APACHE II score, Charlson Comorbidity Index (CCI), emergency status), surgical and medical complications, and cause and time of death. In our patients, the mean CCI score was 3.00\(\pm\)0.81, while the mean APACHE II score was 38.71\(\pm\)4.07. The mean expected mortality was 88.22\(\pm\)7.23.

Discussion
Although ERCP is a minimally invasive procedure, it carries a significant risk due to both anesthetic interventions outside the operating room and the presence of comorbidities and advanced age. The selection of eligible patients is the most important measure for prevention of complications. History of acute pancreatitis within prior weeks, previous MI, insufficient endoscopic and surgical experience of the endoscopy operator, history of hypersensitivity against contrast material, poor performance score for surgery, severe cardiopulmonary disorders, bleeding disorders, and anticoagulant use are contraindications for ERCP [8].

In these procedures, which are generally performed with sedoanalgiesia protocols, one should be careful in monitoring monitoring forregarding potential complications, including mortality, regardless of sedation method used [9]. In ASA guidelines, standard monitoring includes assessment of hemodynamic, oxygenation, pulmonary ventilation, and consciousness, and ECG, pulse oximetry, non-invasive blood pressure monitoring monitoring, BIS, and capnography are recommended for these purposes. Several analgesic and anesthetic agents can be used based on the procedure and patient characteristics. ETCO2 monitoring reduces risks since access to the respiratory tract is limited in ERCP [10].

It was has been shown that BIS monitoring monitoring is

Table 1. Risk factors for ERCP and complications

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Anesthesia outside the operating room (physical conditions, monitoring equipment)</td>
<td></td>
</tr>
<tr>
<td>2. Procedure-related (pancreatitis, bleeding, perforation)</td>
<td></td>
</tr>
<tr>
<td>3. Patient characteristics (gender, comorbidities)</td>
<td></td>
</tr>
<tr>
<td>4. Disease-related (history of pancreatitis, presence of Oddi sphincter dysfunction requiring cannulation of pancreatic duct)</td>
<td></td>
</tr>
<tr>
<td>5. Difficulty in access to patient, prone position</td>
<td></td>
</tr>
<tr>
<td>6. Physostigmine-N-butyrylcholinoiodide</td>
<td></td>
</tr>
</tbody>
</table>

Table 2. Characteristics of fatal cases

<table>
<thead>
<tr>
<th>Patient</th>
<th>Age [year]</th>
<th>Gender [F/M]</th>
<th>BMI</th>
<th>ASA</th>
<th>Number of procedure</th>
<th>Duration of procedure</th>
<th>Comorbidities</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>58</td>
<td>M</td>
<td>29</td>
<td>2</td>
<td>1</td>
<td>15</td>
<td>DM, HT, DM, HT, COPD, HT, Smoking, Chole cystitis, DM, CHF, CHF, DM, HT, Hyperthyroidism</td>
</tr>
<tr>
<td>2</td>
<td>86</td>
<td>F</td>
<td>33</td>
<td>3</td>
<td>1</td>
<td>30</td>
<td>DM, HT, DM, HT, COPD, HT, Smoking, Chole cystitis, DM, CHF, CHF, DM, HT, Hyperthyroidism</td>
</tr>
<tr>
<td>3</td>
<td>85</td>
<td>M</td>
<td>30</td>
<td>2</td>
<td>1</td>
<td>30</td>
<td>DM, HT, DM, HT, COPD, HT, Smoking, Chole cystitis, DM, CHF, CHF, DM, HT, Hyperthyroidism</td>
</tr>
<tr>
<td>4</td>
<td>52</td>
<td>M</td>
<td>34</td>
<td>3</td>
<td>1</td>
<td>30</td>
<td>DM, HT, DM, HT, COPD, HT, Smoking, Chole cystitis, DM, CHF, CHF, DM, HT, Hyperthyroidism</td>
</tr>
<tr>
<td>5</td>
<td>95</td>
<td>M</td>
<td>31</td>
<td>3</td>
<td>1</td>
<td>25</td>
<td>DM, HT, DM, HT, COPD, HT, Smoking, Chole cystitis, DM, CHF, CHF, DM, HT, Hyperthyroidism</td>
</tr>
<tr>
<td>6</td>
<td>74</td>
<td>F</td>
<td>19</td>
<td>3</td>
<td>1</td>
<td>20</td>
<td>DM, HT, DM, HT, COPD, HT, Smoking, Chole cystitis, DM, CHF, CHF, DM, HT, Hyperthyroidism</td>
</tr>
<tr>
<td>7</td>
<td>41</td>
<td>F</td>
<td>24</td>
<td>3</td>
<td>1</td>
<td>60</td>
<td>DM, HT, DM, HT, COPD, HT, Smoking, Chole cystitis, DM, CHF, CHF, DM, HT, Hyperthyroidism</td>
</tr>
</tbody>
</table>
more appropriate than scoring systems (Aldrete) in cases where communication with patient is required [11].

In our ERCP unit, standard monitoring with ECG, pulse oximetry, and non-invasive blood pressure monitoring is employed in all patients and a laryngoscope, anesthesia device, oxygen source, defibrillator, emergent drugs, aspirator, and BIS monitoring monitoring are readily available during ERCP. Standard monitoring was performed in all fatal cases who underwent ERCP in our unit, where all physical conditions and equipment are available.

It was has been shown that hypventilation which couldn't be detected by routine monitoring and clinical assessment was detected by capnography in children who underwent GI endoscopy under conscious sedation [12]. Lack of ETCO2 monitoring is one of the limitations of our study.

According to the WHO, chronological age alone isn't a contraindication for ERCP or a risk factor for ERCP-related complications [13]. It has been reported that frequency of failure, hypoxia, and bleeding due to sphincterotomy is increased by advancing age and that clinicians should be more careful forearlier to complications in women [14], although it was shown that ERCP can be safely employed for diagnostic and therapeutic purposes in elderly individuals in addition to infants and, children and elderly individuals [15-18]. Elder individuals have a greater tendency to hypoxia, hypotension, and arrhythmia [19-21].

In our study, 4 of the non-survivors were at an advanced age according to WHO criteria. Of these, 3 patients died due to sepsis while one patient died due to acute myocardial infarction. It is well-known that obesity carries risk due to physiopathological (cardiac and respiratory) changes. Although there is no study evaluating the relationship between sedoanalgesia and BMI, it is obvious that obesity comprises represents an additional challenge in the semi-prone position for the anesthesiologist. In our study, presence of BMI > 30 in the 4 patients who died suggests that obesity can be an independent risk factor for mortality in ERCP.

Although female gender comprises is a risk factor for surgical complications, it was reported that the results may change in a larger sample size [4]. There are studies reporting that gender is no risk factor [22,23]. In our study, there was no significant difference in gender (3 female and 4 male). We think that our sample size is too small to draw a conclusion.

Another parameter that may influence on mortality is ASA risk scoring. It is widely used in surgical practice in order to identify risk for sedation and anesthesia; however, it is inadequate to determine risk in ERCP procedures and can be misleading. In our study, 4 of 7 patients had ASA III score with expected mortality of 1.8-4.3% whereas 2 had ASA II score with expected mortality of 0.27-0.40%. A fatal course despite low expected mortality was attributed to the fact that expected risk in ERCP is more loosely related to specific complications which that aren't included in the ASA scoring [24]. The APACHE II (Acute Physiology and Chronic Health Evaluation) scoring system is based on worst or most critical physiological and laboratory parameters within the first 24 hours. It is used in adults and provides information regarding estimated mortality rate. In our study, among the 7 patients who died, the minimum APACHE II scores ranged from 31 to 42. The was 31 whereas maximum score was 42 among 7 patients died. The mean APACHE II score was 38.71±4.07 and the mean expected mortality was 88.22±7.23 (Table 3).

The CCI (Charlson Comorbidity Index) is a scale for assessment of comorbid condition plus an additional one point for every 10 years after 40 years of age. In our study, the CCI was moderate in 2 and severe in 5 cases. The Mmean CCI was 3.00±0.81 among patients. APACHE II and CCI were considered to be more significant than ASA score as a mortality index in elective ERCP procedures. We think that APACHE II and CCI can provide more accurate guideline for prediction of mortality in ERCP procedures. Repeated ERCP procedures due to failure or indication can comprise a risk for post-ERCP pancreatitis and perforation. In adults, endoscopy accounts for 75% of esophageus perforations. The distal esophagus adjacent to the cricopharyngeal muscle is the most commonly involved portion. On a CT scan, pneumomediastinum, mediastinitis, and contrast material extravasation can be seen. Pleural effusion or pneumothorax may develop within 12-24 hours [5]. In our study, 2 patients underwent repeat ERCP (third procedure) in emergent conditions. Of these, one patient was admitted to the ICU due to intraoperative respiratory distress, diffuse subcutaneous emphysema, and pneumothorax and another patient due to severe dysrhythmia and respiratory arrest. The patient with pneumothorax died due to septic shock in on the hour 48 after the procedure while the patient with respiratory arrest died due to acute myocardial infarction in on the hour 24 [25].

<table>
<thead>
<tr>
<th>Time of death</th>
<th>Cause of death</th>
<th>Patient 1</th>
<th>Patient 2</th>
<th>Patient 3</th>
<th>Patient 4</th>
<th>Patient 5</th>
<th>Patient 6</th>
<th>Patient 7</th>
<th>Mean±SD</th>
</tr>
</thead>
<tbody>
<tr>
<td>Day 12</td>
<td>AMI</td>
<td>36</td>
<td>42</td>
<td>38</td>
<td>41</td>
<td>41</td>
<td>42</td>
<td>31</td>
<td>38.71±4.07</td>
</tr>
<tr>
<td>Day 2</td>
<td>Sepsis</td>
<td>85.1</td>
<td>93.2</td>
<td>88.4</td>
<td>92.2</td>
<td>38.9</td>
<td>93.2</td>
<td>73.3</td>
<td>88.22±7.23</td>
</tr>
<tr>
<td>Day 14</td>
<td>Sepsis</td>
<td>3 Severe</td>
<td>4 Severe</td>
<td>3 Severe</td>
<td>3 Severe</td>
<td>4 Severe</td>
<td>2 moderate</td>
<td>2 moderate</td>
<td>3.00±0.81</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Emergent</th>
<th>Surgical complication (Pneumothorax)</th>
<th>Respiratory arrest</th>
<th>Severe dysrhythmia</th>
</tr>
</thead>
<tbody>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
<tr>
<td>+</td>
<td>+</td>
<td>+</td>
<td>+</td>
</tr>
</tbody>
</table>

Table 3. APACHE II, CCI, surgical and medical complications, and cause and time of death in fatal cases.
formed [26]. It has been was reported that an endoscopy opera-
tor should complete at least 180 procedures in order to perform
ERCP safely [61]. Our ERCP unit is an academic clinic providing
education and ERCP is performed under the supervision of ex-
perienced endoscopy operators.

Hyoscine-N-butylbromide is an anti-cholinergic agent that is
widely used to achieve duodenal relaxation during ERCP and
may comprise a risk for tachyarrhythmia and anaphylaxis. In
a study of 1177 cases, Christensen-Cristian et al. evaluated
complications of ERCP and reported that Hyoscine-N-butyl-
bromide doses >40 mg are a risk factor for complications in
multivariate analysis [27]. Özgür et al. observed ventricular
tachycardia, severe hypotension, and reversible AMI after 4
doses (20 mg; IV) of Hyoscine-N-butylbromide [28]. In our study,
we also observed AMI after intravenous Hyoscine-N-butylbrom-
ide administration (>40 mg) and the patient died.

Infections following ERCP are the most important frequent
causes of procedure-related morbidity and mortality. Four of
the 7 fatal patients (90.33%) of total ERCP patients) died due to
surgical complication and subsequent sepsis in our study.
Tachycardia, hypotension and enhanced sympathetic activity
may trigger myocardial ischemia or even AMI in patients at risk.
The Remaining 3 patients (90.20% of total ERCP patients) died due to severe dysrythmia and dyspnea followed by AMI
(non-specific complication) in our study [5]. Of the 7 fatal cases, 4 were emergent cases. Of these, 2 patients died due to AMI
including one patient who died during the procedure. We think
that this outcome might be attributed to emergent conditions.

In a review including 21 studies (16,685 patients), 6.85 of pa-
tients had specific complications with a mortality rate of 0.33%.
In another review including 14 prospective studies (12,973 pa-
tients), non-specific complications were assessed. It was found
that 1.33% of patients had non-specific complications with a
mortality rate of 0.87% [29]. In agreement, Consistent with the
literature, the mortality rate was 0.47% among the 1471 pa-
tients in our study.

In conclusion, one should be careful about standard anesthesia
monitoring during the ERCP procedure. In selecting patients, physical conditions should be carefully balanced against risk
factors that may increase mortality regardless of sedation method
used. In conclusion, one should be careful in standard
monitoring and patient selection in addition to physical conditions
against risk factors that may increase mortality regardless of sedation method used in ERCP which is an out-of-
operating room anesthesia procedure. The patients should be
informed about the risks ofregarding mortality and potential
complications by taking comorbidities into account. We think
that using the APACHE II score and CCI rather than the ASA
score can be more effective for predicition of mortality.

Competing interests
The authors declare that they have no competing interests.

References
of 2,715 cases performed by a single endoscopist. Ann Gastroenterol 2014; 27:
65-72.
2. Stockland AH, Baron TH. Endoscopic and radiologic treatment of biliary disease.
In: Gastrointestinal and liver disease. Eds: Feldman M, Friedman LS, Lawrence JB.
4. Santaja U, Goren I, Sendov A. Therapeutic ERCP complications in their risks factors:
tek merkezi prospektif çalışma. Akademik Gastroenteroloji Dergisi 2006; 5.
5. Koçak E, Filik L. Endoscopic retrograde cholangiopancreatography complica-
6. Jowell PS, Baille J, Branch MS, Affronti J, Browning CL, Bute BP. Quantitative as-
sessment of procedural competence. A prospective study of training endoscopic
guideline: The role of ERCP in diseases of the biliary tract and pancreas. Gastroint-
8. Baille J. Indications for and contraindications to ERCP. In: ERCP Book, Eds Todd
9. Sargon M, Santaja TB, Borazan H, Otelcioglu Ş, ŞCP Uygulancak Pediatrik Has-
sedation and analgesia by nonanesthesiologists. A report by the American society
of Anesthesiologists task force on sedation and analgesia by non Anes-
11. Motas DA, Mc Dermott NB, Vanisickle T, Friesen RH. Depth of consciousness and
dep deep sedation attained in children after medical sedation after a stomach surgery.
12. Lighthial J, Sethna NF, Hoa DA, Donovan TM, Fox W. Apolit study of end
Brough, WA. Are complications of endoscopic sphincterotomy age related? Gut
1997; 41: 545-8.
da endoskopik retrograd kolangiopankreatografi, işlemlinin etkinlik ve güvenirliği.
15. Derkx HHH, Hubregtse, K & Taminiau, JAM. The role of endoscopic retrograde
16. Guelrud, M, Mucjica, J, Jaen, D, Plaz, J & Arias, J. The role of ERCP in the diagno-
sis and treatment of idiopathic recurrent pancreatitis in children and adolescents.
17. Mitchell RM, O’Connor F, D’Arcy W. Endoscopic retrograde cholangiopancrea-
tography is safe and effective in patients 90 years of age and older. Alimen
for acute cholangitis in patients 90 years of age and older. Aliment Pharmacol
endoscopic practise for the elderly. American Society for gastrointestinal endo-
ards of practise Committee ASGE guideline modifications in endoscopic practise
21. Ekstein M, Gavish D, Enr I, Weinebrunna AA. Monitored anesthesia care in the
tions of diagnostic and therapeutic ERCP: a prospective multicenter study. Am J
of complications after diagnostic ERCP and effect of comorbidities. Gastroenterol
tory for post-ERCP pancreatitis in high-and low-volume centers and among expert
and non-expert operators: a prospective multicenter study. Am J Gastroenterol
factors for complications following ERCP results of a large-scale, prospective
28. Özgür et al. Karakelle N, Özgur NG, Hyoscine-N-butylbromide induced ven-
tricular tachycardia during ERCP. Journal of Anaesth. Clinical Pharmacology 2014; 30:
118-9.

How to cite this article:
Bakan N, Karacen G, Tomruk SG, Akçay ME, Yanik S, Yildirim D, Ozdil K. Patients
with Mortality After Endoscopic Retrograde Cholangiopancreatography. J Clin Anal