

## Risk factors for complications and mortality related to endoscopic procedures in adults

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### Abstract

**Background / study aims :** The objective of this study is to identify and describe risk factors and complications in endoscopic procedures.

**Methods :** This review presents the complications and the accompanying risk factors that were described in the selected full-text articles. The relevant full-text articles were found in Pubmed, ISI Web of Science and the CINAHL database.

**Results :** The search resulted in 238 abstracts, 50 of which were finally selected for full-text analysis.

The different types of endoscopic procedures each have specific complications, but bleeding and perforation occur in all procedures. It was found that bleeding, perforation, cardiovascular and respiratory complications were common complications.

Furthermore, morbidity and mortality have been associated with risk factors such as older age, high ASA class and sedation.

**Conclusion :** Endoscopy is not without risk, although the prevalence of complications is low. Most complications seen in this analysis, are linked to known risk factors. Some complications might be preventable or avoidable, given a more systematic and comprehensive approach pre-, per- and postprocedural. The creation and implementation of an endoscopic safety checklist could be an important supportive tool in lowering complications. (*Acta gastroenterol. belg.*, 2016, 79, 39-46).

**Key words :** complications, mortality, endoscopy, adults, risk factors.

### Introduction

The current use of endoscopic procedures covers a wide range of diagnostic and therapeutic indications. It has led to improvements in diagnosing complex diseases. Therapeutically, it has created an alternative to sometimes high-risk surgical procedures.

This article focuses on the risk factors that influence procedure-related mortality and/or morbidity, including sedation.

We aim to identify the most common risk factors, as well as the factors with the biggest impact on patient safety and patient comfort. Therefore, we aimed to identify potentially avoidable complications which may be caused by these risk factors, so that in a next step preventive measures can be taken to anticipate the risk factors to the greatest possible extent, resulting in a lower occurrence of complications. The next step is to try to minimize the potential impact of those risk factors. Simultaneously, complications associated with those risk factors can also be avoided.

Once these risk factors are found, standard operating procedures (SOP) and specific guidelines can be created or implemented in order to minimize the risk of compli-

cations during or when preparing for endoscopic procedures (1,2).

### Methods

#### Search strategy

The search for relevant literature regarding risk factors and complications in endoscopy was conducted in 3 renowned scientific databases : Pubmed, ISI Web of Science and the CINAHL database containing full texts (EbscoHost). A combination of the following key terms was included in the search : sedation or anesthesia ; mortality or morbidity ; complications ; medical error ; risk factors and several types of endoscopic procedures. The search for articles was performed over the time period of March-April 2014.

#### Article Selection

Articles were selected on relevance for complications and risk factors in endoscopic procedures.

The selection consists of prospective observational studies (medical file extractions, questionnaires), reviews, randomized trials and retrospective analyses.

Only full-text articles that were accessible to the authors, written in English and published within the last 10 years (2005-2014) were included. Pediatric populations were not included, neither were case reports and animal study models.

#### Quality assessment

The selected articles were independently assessed by the 3 reviewers (1 practicing gastroenterologist, 1 physician working as chief quality officer and 1 Master of Biomedical Science).

The cut-off line defined by the study team was that articles had to be selected by a minimum of 2 reviewers (based on abstracts). Quality assessment was done by means of the CASP checklists (3). A score was given to each article ; only articles with a scoring percentage > 60% were included.

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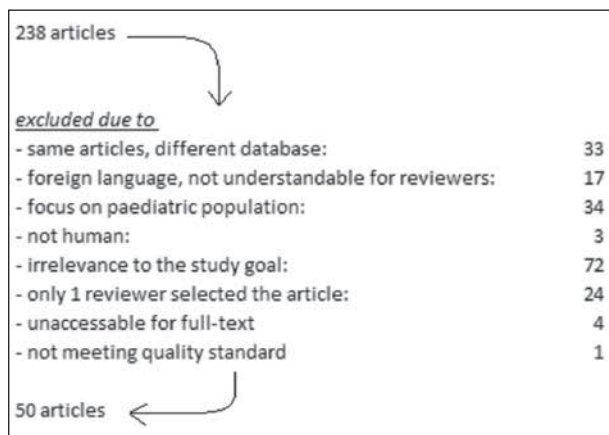


Fig. 1. — Selection of full-text articles

### Data extraction

All full-text articles were read by at least 2 reviewers. The following information was recorded in an evidence table for all articles: study team reference, first author, publication year, title, country, duration of trial (months), methods, quality assessment, patient specifications, intervention and, most importantly, results and conclusions.

The outcome variables we aimed to measure included all relevant complications and risk factors leading to morbidity and mortality in endoscopic procedures. The risk factors, i.e. the primary outcome measures, are a key component to assess the possibility and probability of complications.

### Results

A total of 238 potentially relevant articles were listed. After the critical assessment of titles and abstracts 51 papers were selected for full-text evaluation (Fig. 1). After the quality evaluation 1 article was not included.

Major complications in endoscopic procedures are relatively uncommon and most of the complications are minor without post-procedure effects for the patient.

#### Complications related to procedures

In this article, following procedures are highlighted: endoscopic retrograde cholangiopancreatography (ERCP), gastrointestinal (GI) procedure, endoscopic ultrasound (EUS) and bronchoscopy (Table 1). The most common complications seem to be occurring roughly in all types of procedures, although there is a distinct relation between risk level and type of procedure.

Table 1 shows that each type of endoscopic procedure has its specific complications, for instance pneumothorax in bronchoscopy or cholangitis and pancreatitis in ERCP. Bleeding and perforation however, are 2 complications that have been described frequently in all types.

The American Society of Anesthesiologists (ASA) class and high BMI were seen to be associated with

adverse events during several types of endoscopic procedures (4,5). A higher ASA class has been identified as a risk factor for abnormal heart rates, hypotension and hypoxic events during GI procedures (6-11).

ERCP is regarded as the endoscopic procedure associated with the highest risk of complications and is considered to be one of the most complex endoscopic procedures. Several studies showed complication rates between 5% and 11.6%, and a mortality rate between 0.1 and 1.4% (4,12,13). Mortality during ERCP is usually related to the severity of the disease and underlying malignancies (14).

In general, the most important risk factors that could be attributed to ERCP-related complications are age and physical status (the ASA class) (4). Minor complications are usually transient and related to sedation (14). Examples of these frequent complications include bleeding, hypotension, perforation, cholangitis and pancreatitis (4, 7,15-20).

Upper and lower GI endoscopy are considered safe with a complication rate of less than 1%, 50% of which are cardiovascular complications, e.g. brady- and tachycardia, hyper- and hypotension and hypoxaemia. Bleeding, infection and perforation also occur more frequently.

Co-morbidity plays a role as a risk factor that can lead to complications in GI endoscopy (6,21-24).

EUS and bronchoscopy both have bleeding and perforation as frequently noticed complications (12,16,25-29). Pneumothorax is a complication which specifically is found during bronchoscopic procedures (27-30).

Complications are possible in all endoscopic procedures and occur not only peri-procedural, but also pre- or post-procedural. Looking further into pre-procedural complications, fasting and bowel preparation may for example lead to dehydration, thirst, nausea, vomiting, acute renal failure, dizziness, drowsiness and hypotension) (3,8,20,24,31).

Few complications result in mortality. Mortality in endoscopy has reported rates of 0.012% up to 0.5%, and is considered rare in endoscopy, especially when it comes to diagnostic or screening endoscopic procedures; it is more frequent in therapeutic procedures (9,20,23,32,33). Mortality risk factors which have been described include male gender, older age, co-morbidity and a high ASA class (3,11,21).

Operator inexperience has been named as a relevant risk factor for complications (4,6,10,11,25,31,34). Significant differences in procedure length with a trainee (longer) have been reported, and along with that, significant more complications (4.5% vs 1.2%) when pulmonary endoscopic procedures were performed by a trainee (28). Schreiner *et al.* found that part of this greater percentage of complications can be attributed to a longer procedure time, associated with the higher sedation dosage (35). On the other hand, giving lower doses of sedation could lead to a significant increase of patient intolerance. However, it has been described this could be without a significant increase in adverse events (34,36).

Table 1. — Complications (alphabetical) versus specific endoscopic procedures

Complications	Procedure	ERCp	GI endoscopy	EUS	bronchoscopy
abdominal pain			v (50)	v (12)	
acute renal failure		v (15)	v (50)		
apneu			v (15,50)		
appendicitis			v (37)		
arrhythmia			v (21,50)		
aspiration			v (22,47)		
asthma					v (27,28)
bleeding		v (4,15-18)	v (33,37,38,45,47-49)	v (12,16,25)	v (26-29)
bradycardia		v (7,18)	v (7,8,40,42,51,52)	v (51)	
chipped teeth		v (16)		v (16)	v (28)
cholangitis		v (4,15,17-19)			
COPD exacerbation					v (28)
coughing			v (31)	v (31)	v (30)
dehydration			v (50)		
delirium			v (50)		
diverticulitis			v (37)		
duodenal tear		v (18)	v (37)		
dyspnoe					v (30)
extravasation		v (17)			
fever					v (30)
haemoptysis					v (30)
heart failure		v (17)			v (27,29)
hyperglycemia			v (50)		
hypertension		v (7)	v (7,21,36,42,49,50)		
hypervolemia			v (50)		
hypotension		v (7,16,17)	v (7,20,34,36,40,42,43,47,49,52)	v (20,51)	
hypoxemia		v (7,44)	v (6,7,9,21,36,40)	v (12,25)	v (46)
hypoxia		v (18)	v (33,34,47,49,50,52)		v (26)
infection			v (45,48-50)	v (12,25)	v (28)
methemoglobinemia		v (5)	v (5)		v (5)
nausea			v (50)		
oedema					v (27,29)
oxygen desaturation		v (20,44)	v (20,51,52)	v (20,51)	v (29)
pancreatitis		v (4,15,17,18)		v (12,25)	
perforation		v (15-17)	v (33,37,38,45,47-51)	v (12,16,25,51)	v (27,29)
peritonitis			v (48)		
pneumonia			v (38,40,50)		v (27)
pneumothorax			v (37)		v (27-30)
post-polypectomy syndrome			v (37,48)		
respiratory depression		v (32)	v (32,37,50)		v (27)
respiratory failure					v (28)
seizure					v (28)
shock			v (47)		
sore throat					v (30)
tachycardia		v (7,17)	v (7,8,40,42,47)	v (12)	
vasovagal syncope			v (47,50)		
vomiting			v (50)		

() = reference to be found in reference list.

### Complications related to sedation

Sedation itself can be a risk factor for developing complications (7,11,13,17,20-22,31,32,37-39). The risk for major complications (such as perforation and bleeding) may increase due to oversedation, since this can blunt the pain response. Sarkar *et al.* have researched the effect of creating a guideline towards safe sedation prac-

tices by decreasing the administration of sedative agents. This logically resulted in a significant increase of patient intolerance without, however, a significant increase in adverse events (47).

Propofol is among the most frequently used agents, due to the short recovery time and has been associated with lower complication rates than traditional sedative agents (4). The mean time to sedation is shorter with

propofol, while the depth of sedation is greater. Patients receiving propofol reach full recovery more quickly and it was concluded that they are discharged sooner (39).

It is generally considered that propofol in the right dosage is a safe way to sedate (elderly) patients, although complications such as haemodynamic and respiratory depression still occur (25,40). Rex *et al.* described that the risk of complications during propofol sedation was deemed greater during upper GI endoscopic procedures than during colonoscopy. This significant difference was possibly the result of a deeper average level of sedation during upper endoscopy (41).

Several trials described nurse administered propofol sedation (NAPS), which was considered safe, provided a strict protocol is followed and proper training in airway management and respiratory support is given (4,38,39,42, 43).

#### *Most common complications*

The most common complications described in literature include bleeding, perforation, cardiovascular and pulmonary complications (Table 2). A more detailed description of these complications can be found below.

#### **Bleeding**

Bleeding has been identified as an important complication with numerous associated risk factors, such as age, co-morbidity (e.g. bleeding was significantly more common in malignant airway disease, compared to benign airway disease (40)), and experience of the physician (25, 26,45). As described above, the type of procedure is also considered to be an associated risk factor. Bleeding rarely occurs in the setting of a purely diagnostic examination, but has been reported in up to 1 to 2% of therapeutic cases (46).

On the other hand, factors such as being female and analgesic/sedative premedication have been shown to be protective against bleeding (19).

#### **Perforation**

This complication occurs frequently with various types of endoscopic procedures, but is described especially in gastrointestinal procedures (33,37,38,45,47-49). The overall perforation rate ranges widely between 0.03-0.3% (19,46). It is a serious complication often requiring surgical intervention. Perforation may be due to barotrauma or direct mechanical trauma (3). Risk factors for this complication are older age, co-morbidity, operator inexperience, type of procedure and sedation (22,25,39, 45,49).

#### **Cardiovascular complications**

Cardiovascular complications are the most described and frequently occurring complications in endoscopy (Table 2). During endoscopic procedures, both tachycardia and bradycardia are seen. Other cardiovascular complications are hypertension and hypotension, syncope, shock or cardiac failure.

Tang *et al.* described that taking anti-hypertensive medication has not been associated with procedural hypotension. Therefore, it was not advised to stop anti-hypertensive medication prior to the endoscopic procedure. Their results suggested that the bowel preparations, prior to a colonoscopy, could lead to lower pre-procedural blood pressure (BP) (36).

Hypotension was also significantly more frequent in patients with acute gastrointestinal (GI) bleeding, compared to the non-bleeding group (8.3% vs 3.3%); same as for higher heart rate and lower systemic BP in bleeding patients at start of procedure (39). Female gender (According to Vargo *et al.*, due to longer colon in female, lesser intra-abdominal fat, larger pelvic cavity, less muscles which creates more chance of loops) was also considered a risk factor for hypotension (9). Duration of a colonoscopy longer than 30 minutes, is a recognized risk factor for hypotension (due to inexperience, difficult anatomy, therapeutic interventions and poor bowel preparation) (10,11).

#### **Respiratory complications**

Aspiration and pneumonia are mainly found in gastrointestinal endoscopy. Associated risk factors include age, longer procedure time and sedation (11,22,31,49).

Microaspiration could be considered clinically insignificant if it does not result in pulmonary infection or induce prolonged bronchospasm. It has been described that patients who had hiccups during their procedure were at higher risk for cough (31). Much of the coughing that occurs during endoscopy, however, is clinically insignificant.

Pneumonia could be developed under influence of particular sedation methods. Park *et al.* have described this for endoscopic submucosal dissection (ESD), where they found that it may be worth to avoid continuous propofol infusion in elderly men (38).

One of the most common cardiopulmonary complications during endoscopy is hypoxaemia (15). Reported risk factors associated with hypoxaemia include high ASA class, old age, obesity, sedation, hypertension, longer procedure time and co-morbidity (6,7,9,21,45,46, 48). Respiratory failure, respiratory depression, apnea or pneumothorax are the other most commonly seen respiratory complications (9,13,32,35,37,42,45,50).

## **Discussion**

This article highlights the risk factors and complications associated with endoscopic procedures, and the different results and conclusions in the selected articles. It became clear that authors sometimes reached contradicting results and conclusions.

Therefore, we must emphasize that it is difficult to summarize and draw unanimous conclusions. We believe that randomized controlled trials and collecting data of large populations are the best ways to resolve these contradictions.

Table 2. — Complications versus risk factors

Complications	Risk factor	Age	ASA class	high BMI	female gender	male gender	co-morbidity	bowel preparation (incl. fasting)	longer procedure time + operator inexperience	sphincterectomy	type of procedure	hospitalization	topical anaesthetics	sedation	polyp size	anti-coagulation use	substance abuse	emergency	concomitant medication
abdominal pain		v (4,50)			v (4)				v (4,25)	v (4)									
acute renal failure		v (50)						v (50)											
apnea		v (9,45,50)		v (9,35)							v (42)								
appendicitis														v (37)					
arrhythmia		v (10,21,45)	v (10,11)	v (11,21)			v (21)		v (10,11)		v (11)	v (10)		v (11,13,21)			v (21)	v (10)	v (10)
aspiration		v (22)	v (11)	v (11)			v (22)		v (11,31)		v (11,49)			v (11,22,31)					
asthma											v (27)								
bleeding		v (45)					v (26)		v (25)		v (49)			v (17)	v (37,48)	v (48)		v (37)	v (10)
bradycardia		v (10,45)	v (7,10,11)	v (11)					v (10,11)		v (11)	v (10)		v (7,11,39)				v (7,10)	v (10)
cardiac failure		v (45)	v (11)	v (11)					v (11)		v (11)			v (11)					
chipped teeth									v (28)										
cholangitis											v (25)								
COPD exacerbation														v (37)					
coughing									v (31)		v (48)			v (31)					
dehydration											v (49)								
delirium								v (50)			v (50)			v (50)					
diverticulitis								v (50)			v (25)								
duodenal tear											v (18)								
dyspnoe														v (30)					
extravasation														v (17)					
fever											v (25)								
haemoptysis																			
hypertension		v (10,21,45)	v (7,10)	v (21)			v (21)		v (10)			v (10)		v (21,39)			v (21)	v (7,10)	v (10)
hypervolemia								v (50)											
hypotension		v (10,34,45,50)	v (7,10,11)	v (11)			v (52)	v (50)	v (10,11)		v (11,49)	v (10)	v (14)	v (7,11,17,20,39)				v (7,10)	v (10)
hypoxemia		v (6,21,45,46,48)	v (6,7)	v (6,20)			v (6,21)		v (6)		v (9)			v (7,21)			v (21)	v (7)	
hypoxia		v (10,45)	v (10,11)	v (11)			v (26)		v (10,11,34)		v (11,49)	v (10)		v (11)				v (10)	v (10)
infection		v (50)							v (25)		v (49)								
methemoglobinemia		v (5)									v (5)								
nausea								v (50)											
oedema		v (10)	v (10)						v (10)									v (10)	v (10)
oxygen desaturation		v (10)	v (10)				v (23)		v (10)					v (20,39)				v (10)	v (10)
pancreatitis		v (18)							v (25)					v (17)					
perforation		v (22,45)							v (25)		v (49)			v (39)					
peritonitis									v (25,48)										
pneumonia		v (38,45)	v (11)	v (11)		v (38)			v (11,38)		v (11)			v (11,38)					
pneumothorax									v (27,30,37)										
post-polypectomy syndrome																		v (48)	
respiratory depression																			
respiratory failure			v (10)	v (9)		v (9)													
seizure																			
shock																			
tachycardia		v (10,45)	v (7,10,11)	v (11)					v (10,11)		v (29)								
vasovagal syncope		v (10)	v (10)						v (10)		v (11)	v (10)		v (7,11,17)				v (7,10)	v (10)
vomiting								v (14)											v (10)

() = reference to be found in reference list.

Medical complications are still significantly under-reported, which means that the actual number of complications could be a great deal higher than recorded and estimated (48).

Several authors have reported that older age is an independent risk factor for complications related to colonoscopy (6,10,21,22,34,45,48,50) although it has been reported that colonoscopy in elderly patients is safe (17). It is well known from clinical experience that colonoscopies are technically difficult in elderly patients (due to diverticulosis, sharp angulations and relative inability to hold the air) and have higher failure rates in comparison to younger patients. Continuous monitoring of the patient is vital in the procedure for this specific population (6).

Administration of a lower dose of propofol has been associated with a decrease in the frequency of respiratory depression during endoscopic procedures: This can lead to a lower incidence of respiratory complications in older patients (34).

With judicious monitoring and titration, NAPS should be safe even in high-risk patients and older patients. Salminen *et al.* state that anesthesiological assistance is indicated if the patient's general condition deteriorates during the procedure (24). Morbidity and mortality associated with cardiovascular complications due to sedation continue to be a significant concern especially among the elderly where reduced hepatic and renal clearance are common and can prolong recovery after sedation. This may result in an increase in mortality rate in elderly patients (32).

Monitoring does not prevent complications, but does assist in early recognition. Regular monitoring of vital signs reduces the likelihood of adverse outcomes during moderate and deep sedation. Early detection of oxygen desaturation can be achieved by using oximetry during sedation. Martinez *et al.* suggested to have a member of the nursing staff present during the procedure exclusively for the purpose of patient monitoring (51).

Supplementation of oxygen can reduce the frequency of hypoxaemia, cardiac arrest and death (33), but has also been associated with more cardiorespiratory complications due to masking of hypercapnia (10). Cardiorespiratory depression during the recovery period also occurs due to residual sedation. Monitoring by capnography might ensure further safety (38).

An important way to reduce the risk for complications is a pre-procedural check of the patient's medical condition (particularly blood pressure) and the history of previous examinations (1,2). For an elderly population or high ASA class patients, physicians are advised to be extra cautious and have adequate procedures in place in case complications occur. Physicians are well aware of the possible complications during or directly after the procedure, but are not always fully aware of the pre-procedural complications and especially complications that occur post-procedural (> 4 hrs after procedure). To address this lacuna, it should be possible to set up a system of post-procedural monitoring: predefined points

in time at which in-patients can be visited to check on complications (some complications are not directly experienced as such by the patient), and possibly a telephonic consultation for outpatients. This was described by Dang *et al.* where patients received post-procedural follow-up and results showed that if patients were followed up for 48 hours after the (bronchoscopic) procedure, higher complication rates (up to 20.1%) were reported compared to directly after the procedure (30). Grant *et al.* have demonstrated that an electronic record-keeping system for complications can be an effective quality improvement tool (52).

For instance, risk factors of coughing during endoscopy were identified (e.g. longer procedure time due to operator inexperience, sedation, type of procedure) and may suggest situations where increased vigilance is required to prevent microaspiration and potentially prevent post-procedural pulmonary infectious complications (31, 41).

It is also important to provide adequate and relevant information to the patients who are scheduled for an endoscopic procedure. The informed consent form should be adapted to the various endoscopic explorations in an understandable language for non-clinicians. A prospective study of Villa *et al.* found that 20% of the patients did not completely understand the information, with a high percentage of those patients who were aged > 50 years with only primary education (53). This emphasizes the importance of providing information that is understandable for people from all educational levels. It is widely acclaimed to adjust the level to the educational level of an 11-12 year old. There is an increasing tendency to move away from purely giving informed consent to making informed decisions. Informed decision-making allows patients to actively have a say about their treatment. Choosing the sedation to be applied can be a factor that contributes to patient comfort, which can result in a reduction of discomforts and, potentially, fewer complications.

Currently, there are general guidelines in place that can be followed to perform the procedures. Well-known guidelines are the European and American Society for Gastrointestinal endoscopy (ESGE and ASGE) guidelines (1,2). Harmonization is a determining key factor to analyze all risk factors and complications on an objective basis.

## Limitations

The descriptions, conclusions and suggestions presented in this article should be assessed with caution; further research is needed to draw undisputable conclusions.

The exploratory nature of this study is one of its limitations. Further research should be focused on detecting other possible risk factors associated with other (possibly more rare, but nevertheless important) complications. Another limitation is that not all studies under review

used the same setting (e.g. different sedatives), inclusion criteria, sample size etc. Moreover, different values and definitions of “complications” are used in the articles. Due to the differentiation and heterogeneity in the articles, analysis must be closely controlled to rule out bias.

## Conclusion

Endoscopy involves risks, though the prevalence of complications is low.

The available literature describes a further decline in the number of complications when patients are adequately informed, enough well-trained personnel is available to cover all the available knowledge concerning the various endoscopic procedures, and patients are closely followed up after the procedure. Most complications seen in this analysis, are linked to known risk factors. This means complications can be predictable or at least detectable in an early stage, thus preventing permanent damage. Some complications might even be preventable or avoidable, given a more systematic and comprehensive approach pre-, per- and postprocedural. Multicenter registration studies could provide further insights in this matter. The creation and implementation of an endoscopic safety checklist could be an important supportive tool in lowering complications.

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## Note

The search key and evidence table are available from the authors upon request.

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