SEMMELWEIS EGYETEM

DOKTORI ISKOLA

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UNDERRECOGNIZED RISK FACTORS IN ACUTE GASTROENTEROLOGICAL CONDITIONS REQUIRING ENDOSCOPIC INTERVENTION

Ph.D. Thesis

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Budapest

2026

“The present is theirs; the future, for which I really worked, is mine.”

Nikola Tesla

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1. LIST OF ABBREVIATIONS

CI Confidence Interval

DOI Digital Object Identifier

ERCP Endoscopic Retrograde Cholangiopancreatography

GIB Gastrointestinal Bleeding

GRADE Grading of Recommendations Assessment, Development and Evaluation

HI Hemodynamic Instability

HR Hazard Ratio

LGIB Lower Gastrointestinal Bleeding

LOH Length of Hospitalization

M-W Mallory-Weiss

NA Not Available

NVUGIB Non-Variceal Upper Gastrointestinal Bleeding

OR Odds Ratio

PAD **Periampullary Diverticulum**

PEP Post-ERCP Pancreatitis

PRISMA Preferred Reporting Items for Systematic Reviews and Meta-Analyses

PROSPERO International Prospective Register of Systematic Reviews

PUB Peptic Ulcer Bleeding

RCT Randomized Controlled Trial

SD Standard Deviation

QUIPS Quality in Prognostic Studies

UGIB Upper Gastrointestinal Bleeding

VUGIB Variceal Upper Gastrointestinal Bleeding

2. STUDENT PROFILE

2.1. Vision and mission statement

In my vision, interventional endoscopists work in a multidisciplinary environment alongside collaborative partners to improve patient care outcomes in the field and ensure the highest quality of care. By systematically evaluating clinical predictors and procedure-related risks, decision-making becomes more structured, reproducible, and patient-centered. My mission in this work is to contribute to this approach by generating high-quality evidence and translating relevant findings into practical guidance that supports safer and more effective endoscopic care.

2.2. Specific goals

The specific goals of my work were to evaluate clinically relevant risk factors and outcome determinants in acute and interventional gastroenterology through evidence-based synthesis and quantitative analysis. My research focused on identifying simple, readily assessable clinical and anatomical parameters that support objective risk stratification and guide endoscopic decision-making, with the aim of generating structured, clinically applicable knowledge for everyday practice.

2.3. Scientometrics

Number of all publications:	8
Cumulative IF:	30
Av IF/publication:	3.75
Ranking (SCImago; year of publication):	D1: 3, Q1: 8
Number of publications related to the subject of the thesis:	2
Cumulative IF:	7.8
Av IF/publication:	4.4
Ranking (Scimago; year of publication):	D1:1, Q1: 2
Number of citations on Google Scholar:	64
Number of citations on MTMT (independent):	45
H-index:	6

The detailed bibliography of the student can be found on pages 72-74.

2.4. Future plans

In the coming years, my primary professional goal is to complete my advanced training in interventional endoscopy and to obtain board certification in gastroenterology. Building on the international experience gained during my fellowships, I aim to further strengthen my clinical expertise in complex pancreaticobiliary and emergency endoscopic procedures, while continuing to develop a strong international professional network.

Alongside my clinical career, I intend to further expand my academic activity by supervising early-career researchers and strengthening their competencies in clinical research methodology. I plan to continue and complete my ongoing international clinical studies, including the PROSECCO trial (Prophylactic Endoscopic Sphincterotomy in Patients with Acute Biliary Pancreatitis Unfit for Surgery: A Randomized Controlled Clinical Trial), and to initiate additional multicentric, practice-oriented research projects in the field of acute gastroenterology and interventional endoscopy.

My long-term objective is to integrate high-level clinical practice with research leadership and education. I aspire to play an active role in training the next generation of gastroenterologists, fostering international scientific collaboration, and translating research findings into improved clinical pathways and patient outcomes at both national and international levels.

3. SUMMARY OF THE THESIS

Acute gastroenterological conditions requiring urgent intervention demand rapid yet structured clinical decision-making. In these settings, simple and readily identifiable risk factors are often recognized in routine practice but are not systematically incorporated into procedural planning or formal risk stratification. Papilla morphology assessed at the start of ERCP (endoscopic retrograde cholangiopancreatography) and hemodynamic instability (HI) at presentation in acute gastrointestinal bleeding (GIB) represent two such parameters that may substantially influence procedural and clinical outcomes

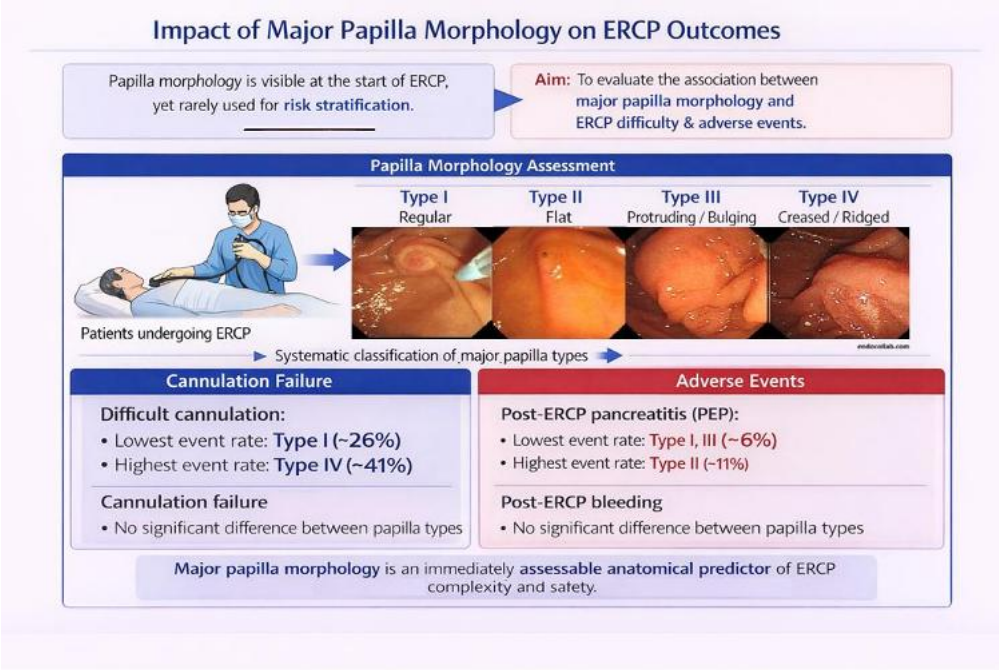
In this thesis, we investigated the role of major papilla morphology in determining the safety and efficacy of ERCP, and the prognostic significance of HI at admission in patients with acute GIB. To address these questions, two systematic reviews and meta-analyses were conducted in accordance with Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) recommendations and the methodological guidance of the Cochrane Handbook, with both protocols prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO).

Across a substantial international evidence base, papilla morphology was found to be associated with ERCP complexity and adverse-event risk. Type I papillae were consistently linked to lower rates of difficult cannulation, whereas type II papillae were associated with an increased risk of post-ERCP pancreatitis. In contrast, HI in acute GIB was strongly associated with worse clinical outcomes, including higher in-hospital and short-term mortality, increased rebleeding rates, and a greater likelihood of requiring surgical intervention.

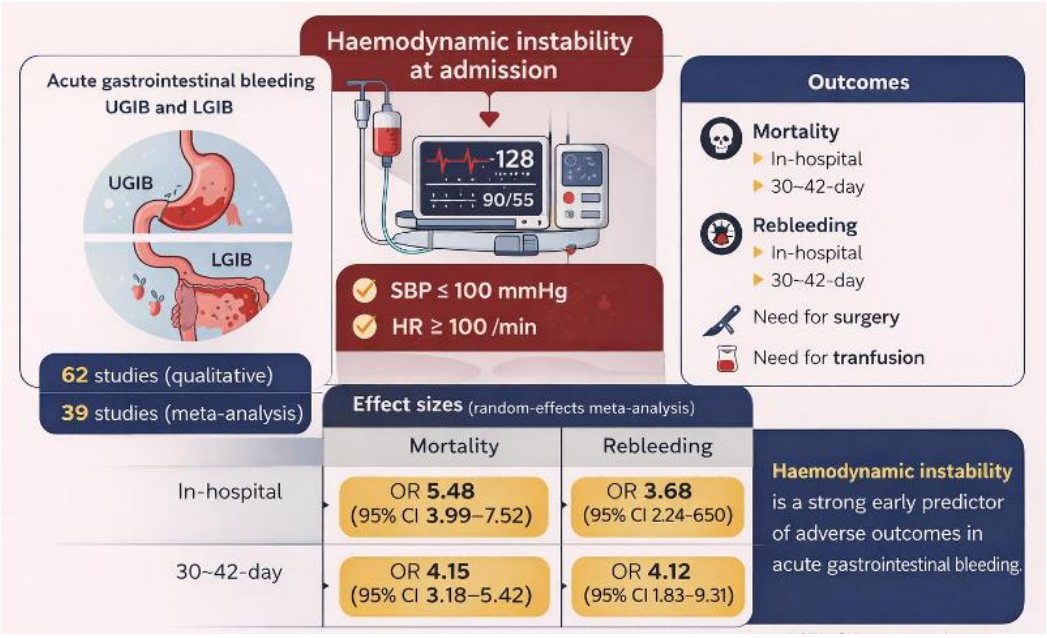
Taken together, these findings indicate that papilla morphology in ERCP and HI in acute GIB constitute clinically meaningful anatomical and physiological risk factors. Their systematic assessment, structured documentation, and integration into endoscopic decision-making pathways may support more individualized, risk-adapted management and contribute to improved patient safety and outcomes in acute gastroenterological care.

4. GRAPHICAL ABSTRACT

4.1. Study 1



4.2. Study 2



5. INTRODUCTION

5.1. Acute gastrointestinal conditions and urgent endoscopic decision-making

Acute gastrointestinal conditions frequently require urgent endoscopic intervention. Despite substantial advances in endoscopic techniques and peri-procedural management, clinical outcomes remain highly variable and are strongly influenced by patient-related and anatomical risk factors that are often underrecognized in routine clinical practice.

Endoscopic retrograde cholangiopancreatography (ERCP) and acute gastrointestinal bleeding (GIB) represent distinct clinical entities that occur in high-risk settings and require rapid endoscopic decision-making. In these scenarios, simple and readily available parameters such as papilla morphology or the presence of hemodynamic instability (HI) at presentation may critically influence procedural success and patient outcomes. The structured integration of these factors into evidence-based endoscopic management strategies remains limited.

5.2. Anatomical risk stratification in ERCP

ERCP is one of the most frequently performed endoscopic procedures for pancreaticobiliary disorders. Despite continuous technical refinement over recent decades, biliary cannulation remains a critical step of the procedure, with reported failure rates of 5–20% even in experienced hands (1). ERCP is also associated with a substantial risk of adverse events, most notably post-ERCP pancreatitis (PEP), which occurs in approximately 10% of procedures and in more than 14% of high-risk patients, with evidence indicating that its incidence has remained largely unchanged over the past decades (2).

Variations in the macroscopic appearance of the major duodenal papilla have long been recognized during routine endoscopic practice, raising the possibility that anatomical factors may influence cannulation difficulty and procedural risk (3). This assumption has been supported by the development of validated endoscopic classification systems and by prospective data suggesting an association between papilla anatomy, cannulation complexity, and adverse events (4, 5).

However, despite the availability of these data, papilla morphology is rarely considered as part of structured procedural planning or formal risk assessment. As a result, its potential role as a readily assessable anatomical risk factor has not yet been consistently translated into structured procedural decision-making.

5.3. Underrecognized risk factors in acute GIB

Acute GIB is a frequent and potentially life-threatening emergency in gastroenterology, with reported mortality rates of 2–10% (6, 7). Early risk stratification is therefore essential, as delayed recognition and inadequate initial resuscitation are associated with increased mortality and higher rates of rebleeding (8).

Approximately 25% of patients presenting with acute GIB develop HI, reflecting significant blood loss and circulatory compromise (9). This condition is easily identifiable at the bedside and is widely perceived as a marker of severe disease. However, despite its frequent recognition in clinical practice, the prognostic relevance of HI has not been consistently defined across studies, and its role in guiding early management decisions remains insufficiently addressed in current guidelines (10-12).

Consequently, HI is often acknowledged but not systematically integrated into structured risk stratification or endoscopic decision-making algorithms. This lack of standardization has contributed to uncertainty regarding its true impact on clinically relevant outcomes, including mortality and rebleeding, in patients with acute GIB.

5.4. Rationale and aims of the thesis

The common challenge across ERCP and acute GIB lies in the lack of structured integration of simple, readily identifiable risk factors into evidence-based endoscopic decision-making. Both papilla morphology and HI are easily assessable parameters that may substantially influence outcomes, yet their prognostic and procedural relevance has not been consistently quantified or standardized. The overarching aim of this thesis is to evaluate underrecognized risk factors in acute gastroenterological conditions requiring urgent endoscopic intervention and to clarify their impact on clinically relevant outcomes.

Through systematic evidence synthesis and meta-analytical approaches, this work seeks to improve the understanding of how anatomical risk profiling in ERCP and early

identification of HI in acute GIB may contribute to more informed clinical decision-making, improved procedural outcomes, and enhanced patient safety.

6. OBJECTIVES

6.1. Study 1 – Morphology of the papilla can predict procedural safety and efficacy of ERCP: a systematic review and meta‑analysis

We aimed to systematically evaluate the available evidence on the role of papilla morphology in ERCP and to clarify its clinical relevance for biliary cannulation outcomes. Therefore, we investigated whether different papilla morphology types are associated with an increased risk of difficult or unsuccessful cannulation and with a higher incidence of post-ERCP adverse events, particularly PEP. We hypothesized that specific papilla morphologies represent anatomical risk factors that predispose to more challenging cannulation and less favorable procedural outcomes during ERCP.

6.2. Study 2 – At admission hemodynamic instability is associated with increased mortality and rebleeding rate in acute gastrointestinal bleeding: a systematic review and meta-analysis

We aimed to systematically evaluate the available evidence on the prognostic role of HI at presentation in acute GIB and to clarify its impact on clinically relevant outcomes. Therefore, we investigated whether the presence of HI or shock at admission is associated with an increased risk of mortality and rebleeding, as well as other adverse outcomes, including the need for surgery, transfusion, and prolonged hospitalization. We hypothesized that HI at presentation represents a strong prognostic factor and is associated with significantly worse short- and medium-term outcomes in patients with acute GIB.

7. METHODS

Two independent systematic reviews and meta-analyses were conducted to address the predefined research questions. Both studies were performed in accordance with the Preferred Reporting Items for Systematic Reviews and Meta-Analyses (PRISMA) statement and the recommendations of the Cochrane Handbook for Systematic Reviews of Interventions (13, 14).

The protocols of the two reviews were prospectively registered in the International Prospective Register of Systematic Reviews (PROSPERO) under the registration numbers CRD42021285727 and CRD42022360894, respectively.

7.1. Information sources and search strategy

7.1.1. Study 1

Three databases — MEDLINE (via PubMed), Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL) — were systematically searched from inception to September 29, 2022. No filters or restrictions were applied. The main parts of the search query included terms related to ERCP and papilla morphology, with the following search key: (papilla) AND (cannulation OR endoscopic retrograde OR ERCP). Additionally, relevant articles were identified by manually screening the reference lists and citation records of all included studies.

7.1.2. Study 2

Three databases, MEDLINE (via PubMed), Embase, and the Cochrane Central Register of Controlled Trials (CENTRAL), were systematically searched from inception to October 22, 2021. We did not apply any filters or restrictions to our search. The main parts of the search query included terms in connection with HI/shock and GIB, with the following search key: (gastrointestinal haemorrhage OR gastrointestinal hemorrhage OR gastrointestinal bleed OR GI bleed* OR GIB OR UGIB OR LGIB OR ((nonvariceal OR non-variceal OR variceal OR varix OR ulcer) AND bleeding)) AND (shock OR ((hemodynamic* OR haemodynamic*) AND (instability OR unstable OR compromised))). In addition, we manually searched for relevant articles and checked the bibliographic reference lists of studies selected for inclusion.

7.2. Eligibility Criteria

7.2.1. Study 1

The condition–context–population (CoCoPop) framework was applied to define eligibility criteria (15). The conditions of interest included difficult biliary cannulation, cannulation attempts, cannulation time, cannulation failure, PEP, and other ERCP-related adverse events (bleeding, perforation, and infection), evaluated in the context of different papilla morphologies. The population comprised adult patients (≥18 years) undergoing ERCP with a native papilla. Randomized controlled trials (RCTs), case–control studies, cross-sectional studies, and cohort studies were considered eligible. Both full-text publications and conference abstracts providing sufficient extractable data were included. Definitions of difficult cannulation, cannulation failure, and post-ERCP adverse events were accepted as reported in the individual studies.

7.2.2. Study 2

The population–exposure–outcome (PEO) framework was applied to define eligibility criteria (15). The population of interest comprised adult patients (≥18 years) presenting with GIB. Studies were considered eligible if they reported outcomes in patients with HI or shock at admission. The primary outcome was mortality, while secondary outcomes included rebleeding, need for surgery, need for transfusion, length of hospitalization (LOH), and the need for rescue endoscopic therapy. Outcomes were assessed separately in upper GIB (UGIB), lower GIB (LGIB), and mixed populations including both UGIB and LGIB patients. Definitions of HI or shock were accepted as reported in the individual studies; based on these definitions, HI and shock were considered synonymous, and the term HI was used throughout this review. RCTs, case–control, cross-sectional, and cohort studies were eligible for inclusion in the systematic review, while only cohort studies were included in the meta-analysis. Only full-text articles were considered eligible.

7.3. Study Selection and Data Extraction

For both studies, all records retrieved from the systematic search were imported into a reference management software (EndNote X7.4, Clarivate Analytics, Philadelphia, PA, USA), and duplicates were removed using automated and manual procedures. Two independent reviewers subsequently screened the remaining records based on title and

abstract, followed by full-text assessment. Inter-reviewer agreement was evaluated at both stages using Cohen's kappa coefficient (κ) (16). Data extraction was performed independently by two investigators using a purpose-designed Microsoft Excel 2016 spreadsheet (Office 365, Microsoft, Redmond, WA, USA).

7.3.1. Study 1

7.3.1.1. Study selection and data extraction

Data were extracted on the first author, year of publication, digital object identifier (DOI), data collection period, study location, number of centers, study design, patient age (reported as mean or median with corresponding standard deviation (SD) or interquartile range), total sample size, number of female patients, number of patients in each papilla morphology category, and data on primary and secondary outcomes reported separately for the different papilla types.

7.3.1.2. Morphology of the papilla

Papilla morphology was classified using the Haraldsson system, the first classification with validated intra- and interobserver agreement (5). According to this system, papillae are categorized into four types: regular (type 1), small (type 2), protruding or pendulous (type 3), and creased or ridged (type 4).

As a secondary analysis, a comparison between the Haraldsson classification and other papilla morphology classification systems identified in the literature was performed. For this purpose, two endoscopists independently reviewed the morphological descriptions and available images reported in the included studies and assigned corresponding Haraldsson papilla types. In cases of disagreement, consensus was achieved through adjudication by a third reviewer. Based on this comparison, additional analyses were conducted.

7.3.2. Study 2

Data were extracted on the first author, year of publication, study location, study design, enrollment period, study population, sample size, patient age, source of bleeding, duration of follow-up, numbers of patients with and without HI or shock at admission, and the definitions of HI or shock applied in each study. Effect estimates, including odds ratios

(ORs) and hazard ratios (HRs) with corresponding 95% confidence intervals (CIs), were also collected.

When multiple publications originated from the same patient cohort, the study reporting the largest sample size was included.

7.4. Risk of Bias and Quality of Evidence Assessment

All assessments were conducted independently by two reviewers. In cases of disagreement, consensus was reached through discussion; if disagreement persisted, a third reviewer was consulted.

7.4.1. Study 1

The risk of bias for each outcome was assessed using the Joanna Briggs Institute Critical Appraisal Checklist for studies reporting prevalence (17). The overall certainty of the evidence was evaluated in accordance with the Grading of Recommendations Assessment, Development, and Evaluation (GRADE) approach (18).

7.4.2. Study 2

The risk of bias for each outcome was assessed using the Quality In Prognostic Studies (QUIPS) tool (19).

7.5. Data Synthesis and Analysis

Statistical analyses were performed by a biostatistician using the R programming language (R Core Team, 2022; version 4.2.1). Forest plots were used to present the results of the meta-analyses. A minimum of three studies was required to perform a meta-analysis.

7.5.1. Study 1

Event rates with corresponding 95% CIs were used as effect size measures. Anticipated between-study heterogeneity was addressed using random-effects meta-analysis to obtain pooled estimates. Publication bias was evaluated by visual inspection of funnel plots, and sensitivity analyses were conducted using the leave-one-out approach.

As multiple papilla morphology subgroups were reported within individual studies, a three-level random-effects meta-analysis was applied to account for the non-

independence of effect size estimates derived from the same study (20). Statistical heterogeneity was quantified using the I^2 statistic, and subgroup differences between papilla morphology types were assessed using the Cochrane Q test. A two-sided p value <0.05 was considered statistically significant.

7.5.2. Study 2

In-hospital mortality, 7-day mortality, and both 6-week and 30-day mortality were pooled. The same analytical approach was applied to rebleeding outcomes. Pooled ORs with 95% CIs were calculated using random-effects models. Between-study heterogeneity was assessed using the I^2 statistic, as described by Thompson and Higgins (21). Publication bias was evaluated by visual inspection of funnel plots and by Egger's test, with additional analyses performed when a potential small-study effect was suspected (22). Sensitivity analyses were conducted using the leave-one-out method. Subgroup analyses were performed in studies in which the bleeding subtype was specified. Additional analyses were conducted in studies defining HI as a systolic blood pressure ≤100 mmHg and/or a pulse rate ≥100/min.

8. RESULTS

8.1. Study 1: Morphology of the papilla can predict procedural safety and efficacy of ERCP: a systematic review and meta‑analysis

8.1.1. Study search and selection

The study selection process is presented in the PRISMA flow chart (see Figure 1). In total, 6,952 records were retrieved from the database search. After the screening and eligibility assessment, 17 studies were retained for the narrative synthesis (3, 4, 23-37), and 14 of these could be incorporated into the quantitative analysis (3, 4, 23, 24, 26, 28-36).

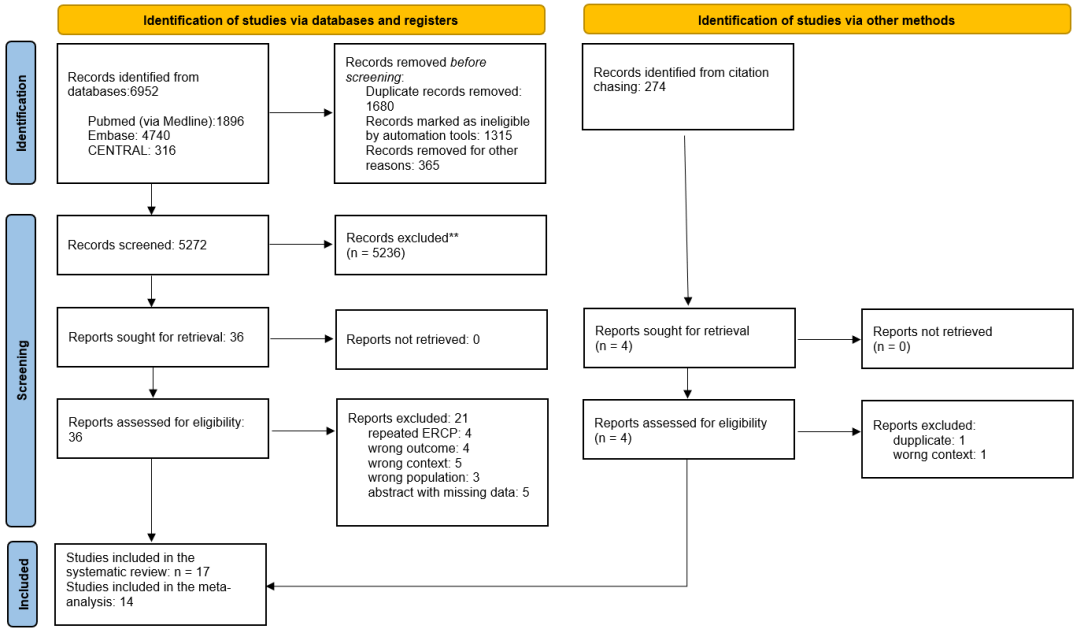


Figure 1. *PRISMA 2020 flowchart representing the detailed systematic search and study selection process (38).*

8.1.2. Basic characteristics of the included studies

The main characteristics of the included studies are summarised in Table 1. The eligible studies were published between 2016 and 2022. Of the 17 studies, 15 followed a cohort design, including eight prospective (3, 4, 23-25, 29, 31, 32) and seven retrospective investigations (27, 28, 30, 34-37). In addition, one case–control study (33) and one cross-sectional study (26) were identified. Thirteen studies were available as full-text articles

(3, 4, 23, 24, 26-29, 31, 33, 35-37), while four were published as conference abstracts (25, 30, 32, 34).

Seven studies applied the Haraldsson classification (3, 4, 26, 28, 31, 33, 34), and a further seven used classification systems that were comparable to it (23, 24, 29, 30, 32, 35, 36). In three studies, the applied classifications were not directly comparable to the Haraldsson system (25, 27, 37). The sample size varied widely across studies, ranging from 72 to 11,090 participants.

Table 1. Basic characteristics of the included articles in Study 1 (38).

Author	Year	Centers	Study type	Age (*:mean; #:median)	Sex (female%)	Number of patients	Classification	Outcomes
Balan et al. (23)	2020	1	prospective cohort	NA	NA	322	Regular: 52% Canard type I 11% Canard type II: 19% Canard type III: 10% Canard type IV: 8%	difficult cannulation cannulation time cannulation attempts post-ERCP pancreatitis, bleeding, infection
Canena et al. (24)	2021	3	prospective cohort	*69.6	56.8%	361	Viana type I: 13% Viana type IIa: 35% Viana type IIb: 30% Viana type IIc:10% Viana type IIIa: 4% Viana type IIIb: 4% Viana type IV: 4%	cannulation failure cannulation time post-ERCP pancreatitis, bleeding, perforation
Chen et al. (3)	2020	1	prospective cohort	*64 (SD: 16.5)	47.5%	286	Haraldsson type I: 41% Haraldsson type II: 9% Haraldsson type III: 22% Haraldsson type IV: 28%	cannulation failure cannulation time post-ERCP pancreatitis, bleeding, perforation, cholangitis
Fernandes et al. (25)	2018	3	prospective cohort	#79	59.4%	106	Leés type I: 50% Leés type II: 32% Leés type III: 12% Leés type IV: 6%	cannulation time
Gutierrez- De Aranguren et al. (26)	2021	1	retrospective cross-sectional	*55 (SD: 20)	66.5%	188	Haraldsson type I: 32% Haraldsson type II: 25% Haraldsson type III: 27% Haraldsson type IV: 16%	difficult cannulation
Haraldsson et al. (4)	2019	9	prospective cohort	66 (SD: 16)	52%	1377	Haraldsson type I: 56% Haraldsson type II: 13% Haraldsson type III: 23% Haraldsson type IV: 8%	difficult cannulation cannulation time post-ERCP pancreatitis

Liu et al. (27)	2021	1	retrospective cohort	NA	NA	11 090	Normal: 44% Thick and long: 11% Peridiverticular: 27% Intradiverticular: 5% Ectopic: 1% Edematous 10% Ulcerative: 2%	difficult cannulation
Mohamed et al. (28)	2021	1	retrospective cohort	NA	51.8%	637	Haraldsson type I: 62% Haraldsson type II: 5% Haraldsson type IIIa: 9% Haraldsson type IIIb: 9% Haraldsson type IV: 3% Type D: 12%	cannulation failure cannulation time cannulation attempts post-ERCP pancreatitis, bleeding, cholangitis or sepsis
Nakeeb et al. (29)	2016	1	prospective cohort	*58.4 (SD: 14.7)	44.4%	996	Normal: 60% Atrophic: 3% Pregnant: 7% Tumour: 7% Redundant: 8% Juxtadiverticular: 8% Small: 6% Long: 1%	post-ERCP pancreatitis
Onilla et al. (30)	2021	1	retrospective cohort	NA	NA	347	Regular protrusion: 57% Small protrusion: 31% Large protrusion: 12% Annular pattern: 72% Unstructured pattern: 11% Longitudinal pattern 11% Isolated pattern: 1% Gyrus pattern: 5%	difficult cannulation, cannulation failure
Quiroga-Purizaca et al. (31)	2022	1	prospective cohort	*51.5 (CI: 48.8-54.1)	68.4%	138	Haraldsson type I: 59% Haraldsson type II: 8% Haraldsson type III: 29% Haraldsson type IV: 4%	difficult cannulation cannulation time cannulation attempts post-ERCP pancreatitis, bleeding, perforation

Sadeghi et al. (32)	2019	1	prospective cohort	*62.3 (SD: 15.5)	51.4%	72	Small: 33% Bulging: 28% Long: 39%	cannulation success
Saito et al. (33)	2022	3	retrospective case-control	*74.9	47.5%	1406	Haraldsson type I: 45% Haraldsson type II: 44% Haraldsson type III: 7% Haraldsson type IV: 4%	difficult cannulation
Thongsuwan et al. (34)	2021	1	retrospective cohort	NA	50.4%	558	Haraldsson type I: 66% Haraldsson type II: 16% Haraldsson type III: 12% Haraldsson type IV: 6%	difficult cannulation cannulation failure post-ERCP pancreatitis, bleeding, infection
Watanabe et al. (35)	2019	1	retrospective cohort	#70	36%	589	Regular protrusion: 12% Small protrusion: 78% Large protrusion: 10% Annular pattern: 67% Unstructured pattern: 7% Longitudinal pattern: 7% Isolated pattern: 1% Gyrus pattern:16% Unclassified pattern: 2%	difficult cannulation cannulation failure cannulation attempts
Zhang et al. (36)	2016	1	retrospective cohort	*75 (SD: 2.2)	42.7%	82	bulging: 44% normal: 22% small: 16% unusual location: 18%	cannulation success cannulation time
Zheng et al. (37)	2020	1	retrospective cohort	NA	46.1%	2385	others:18% villous: 74% granular: 8%	post-ERCP pancreatitis

NA: not available; SD: standard deviation; CI: confidence interval; ERCP: endoscopic retrograde cholangiopancreatography

8.1.3. Quantitative Synthesis

8.1.3.1. Difficult cannulation

Nine studies reported data on the rate of difficult cannulation (4, 23, 26, 27, 30, 31, 33-35), of which eight were eligible for quantitative synthesis (4, 23, 26, 30, 31, 33-35). In analyses restricted to studies applying the Haraldsson classification, difficult cannulation occurred less frequently in type I papillae (26%; CI 18–37) compared with the other papilla types (type III: 35%; CI 25–48; type II: 39%; CI 28–52; type IV: 41%; CI 28–55). Although this difference did not reach statistical significance, the p-value indicated a trend toward higher rates of difficult cannulation in certain papilla types (p = 0.075). Heterogeneity was considerable (total I^2 = 89%; CI 48–98). Sensitivity analyses did not identify outlier studies or relevant changes in the pooled effect estimates (see Figure 2).

A similar pattern, but with a statistically significant difference and no outlier studies, was observed when all studies using various classification systems were included (p = 0.019; total I^2 = 87%; CI 55–96; see Figure 3).

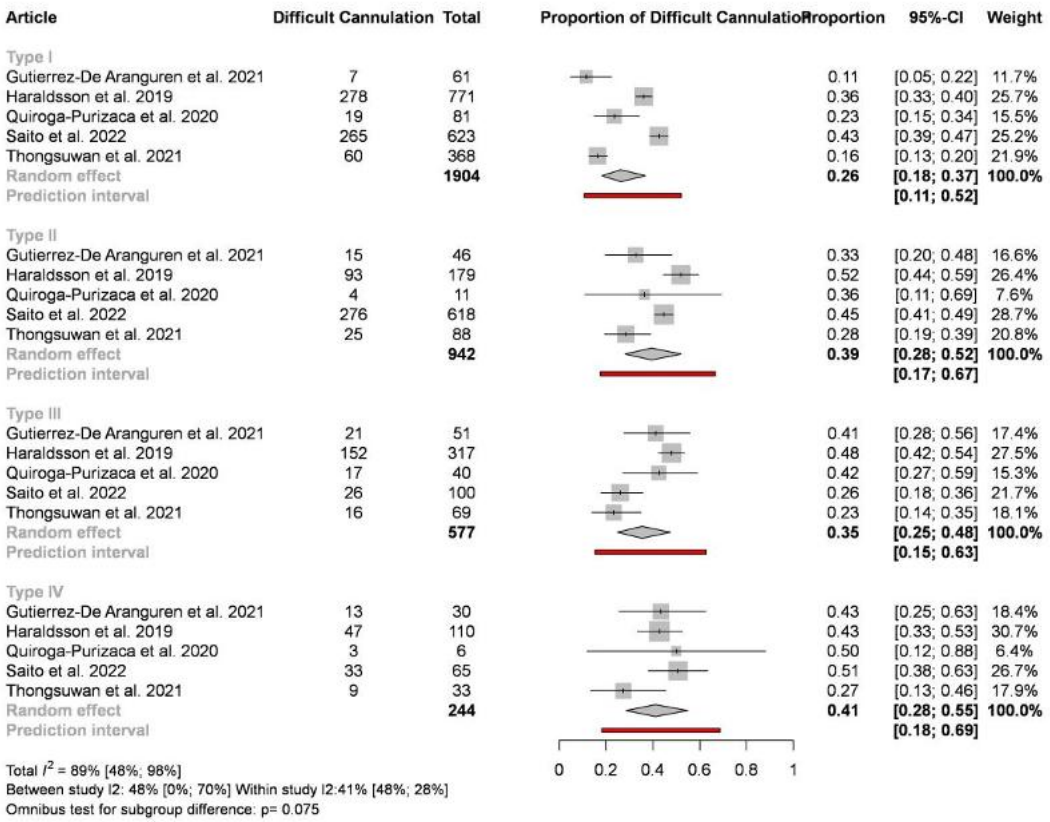


Figure 2. *Forest plot representing the pooled event rate of difficult cannulation in the different papilla types in studies using the Haraldsson classification, showing a lower tendency for difficult cannulation in type I papilla compared to the other papilla types (38). CI: confidence interval.*

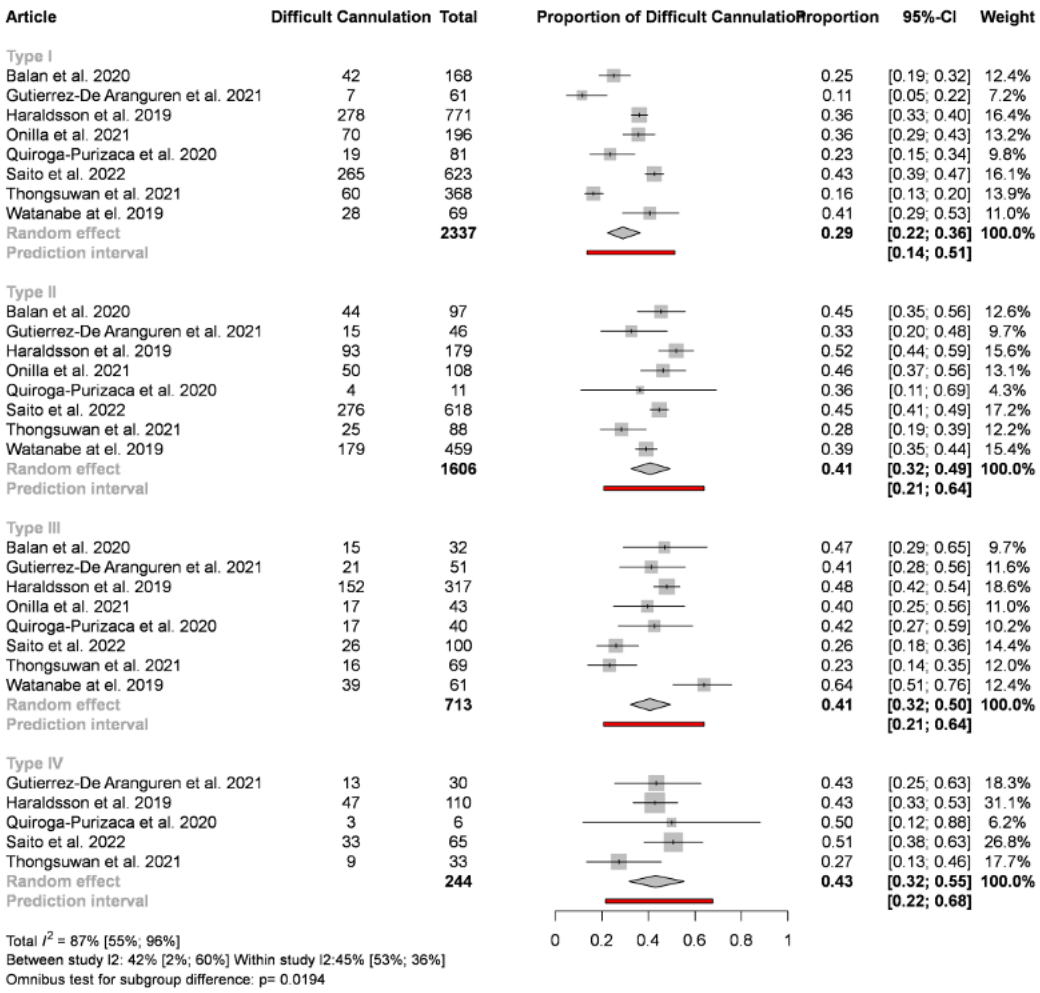


Figure 3. *Forest plot representing the pooled event rate of difficult cannulation in the different papilla types in studies using different classification systems, showing statistically significantly lower rate in type I papilla, compared to the other papilla types (38). CI: confidence interval.*

8.1.3.2. Cannulation failure

Eight studies reported the rate of cannulation failure, all applying the Haraldsson classification or a comparable system (3, 24, 28, 30, 32, 34-36). When the analysis was restricted to studies

using the Haraldsson classification, no statistically significant differences were detected in cannulation failure rates across papilla types (p = 0.262; total I^2 = 61%; CI 0–97; see Figure 4).

When all eight studies were included, the difference became statistically significant (p = 0.047; I^2 = 64%; CI 0–91). In this pooled analysis, cannulation failure occurred most frequently in type II papillae (8%, CI 4–14) and least frequently in type I papillae (3%, CI 2–6; see Figure 5). Sensitivity analyses did not identify outlier studies or relevant changes in the pooled effect estimates.

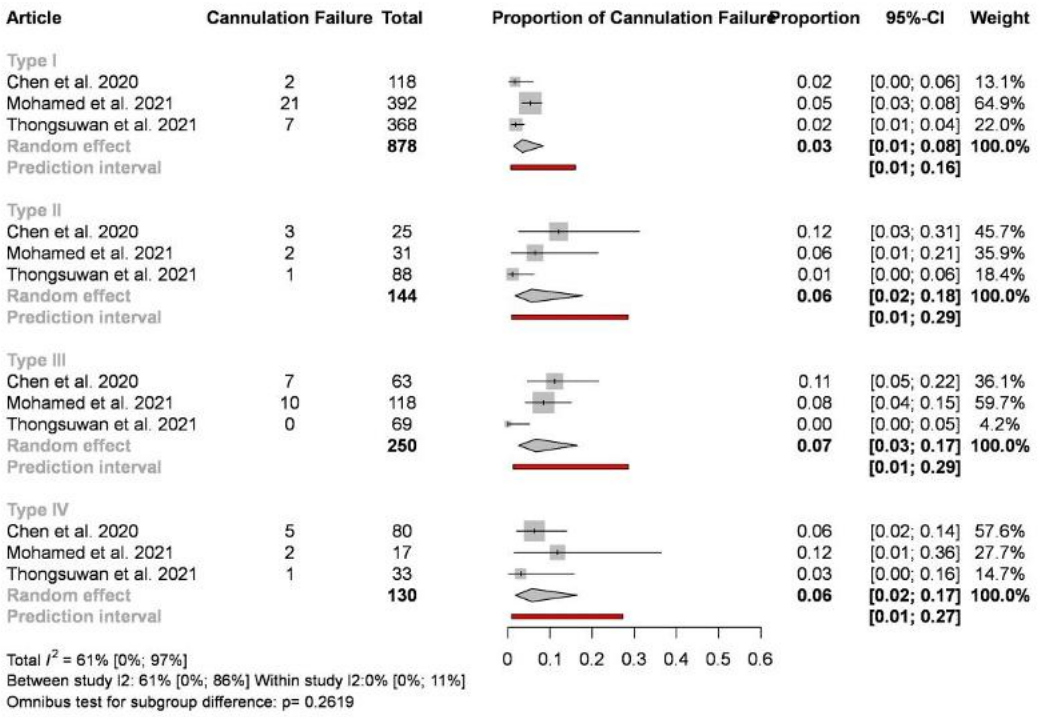


Figure 4. *Forest plot representing the pooled event rate of cannulation failure in the different papilla types in studies using the Haraldsson classification, showing no statistically significant difference in the event rates between the papilla types (38). CI: confidence interval.*

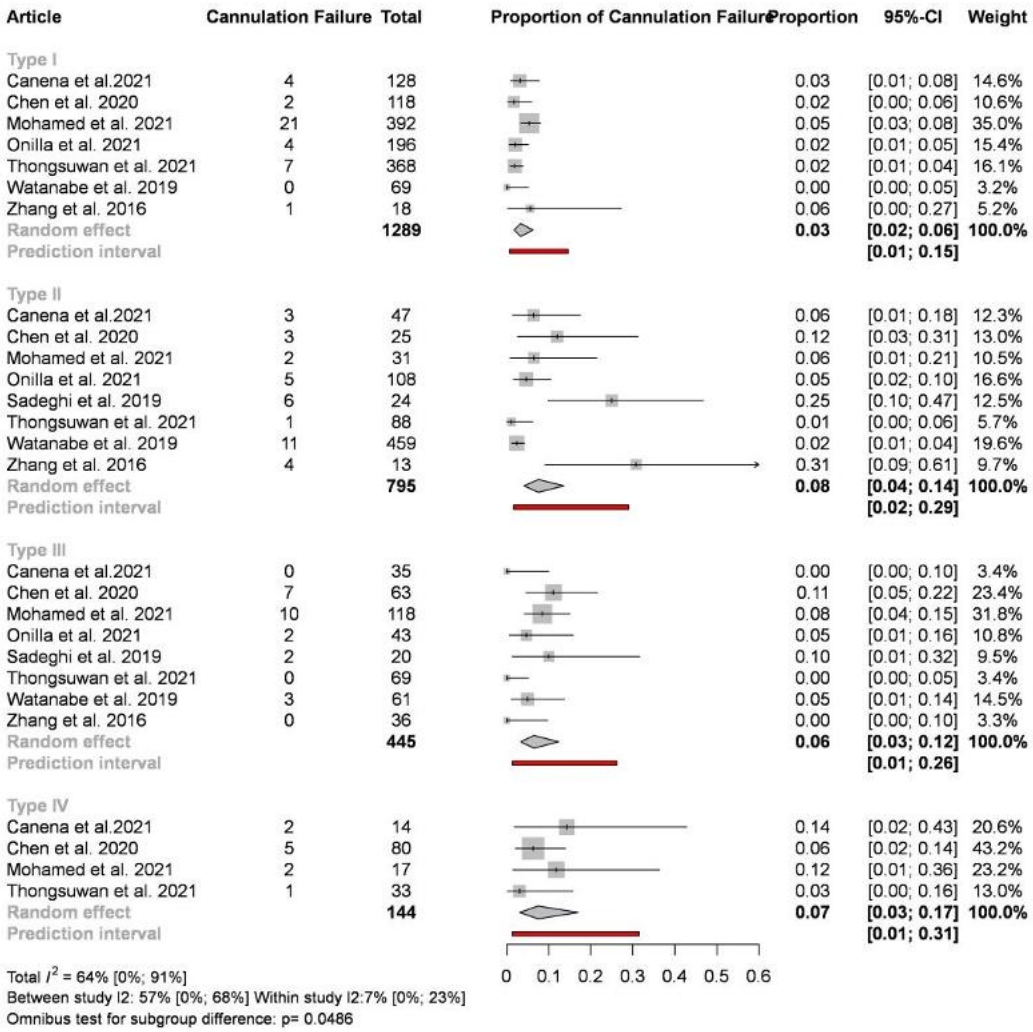


Figure 5. *Forest plot representing the pooled event rate of cannulation failure in the different papilla types in studies using different classification systems, showing statistically significant difference in the event rates between the papilla types (38). CI: confidence interval.*

8.1.3.3. Post-ERCP pancreatitis

Nine of the included studies reported the rate of PEP across different papilla types (3, 4, 23, 24, 28, 29, 31, 34, 37), eight of which were suitable for quantitative synthesis (3, 4, 23, 24, 28, 29, 31, 34). In analyses limited to studies applying the Haraldsson classification, PEP occurred more frequently in type II papillae (11%; CI 8–15) compared with the other papilla types (type IV: 7%; CI 4–12; type I: 6%; CI 5–8; type III: 6%; CI 4–8). This difference was statistically significant (p = 0.0441), and heterogeneity was negligible (total I^2 = 0%; see Figure 6).

When all eight studies using different classification systems were included, a similar pattern was observed; however, the difference between papilla types was not statistically significant (p

= 0.103; see Figure 7). Sensitivity analyses did not identify any influential outliers or relevant changes in the effect estimates.

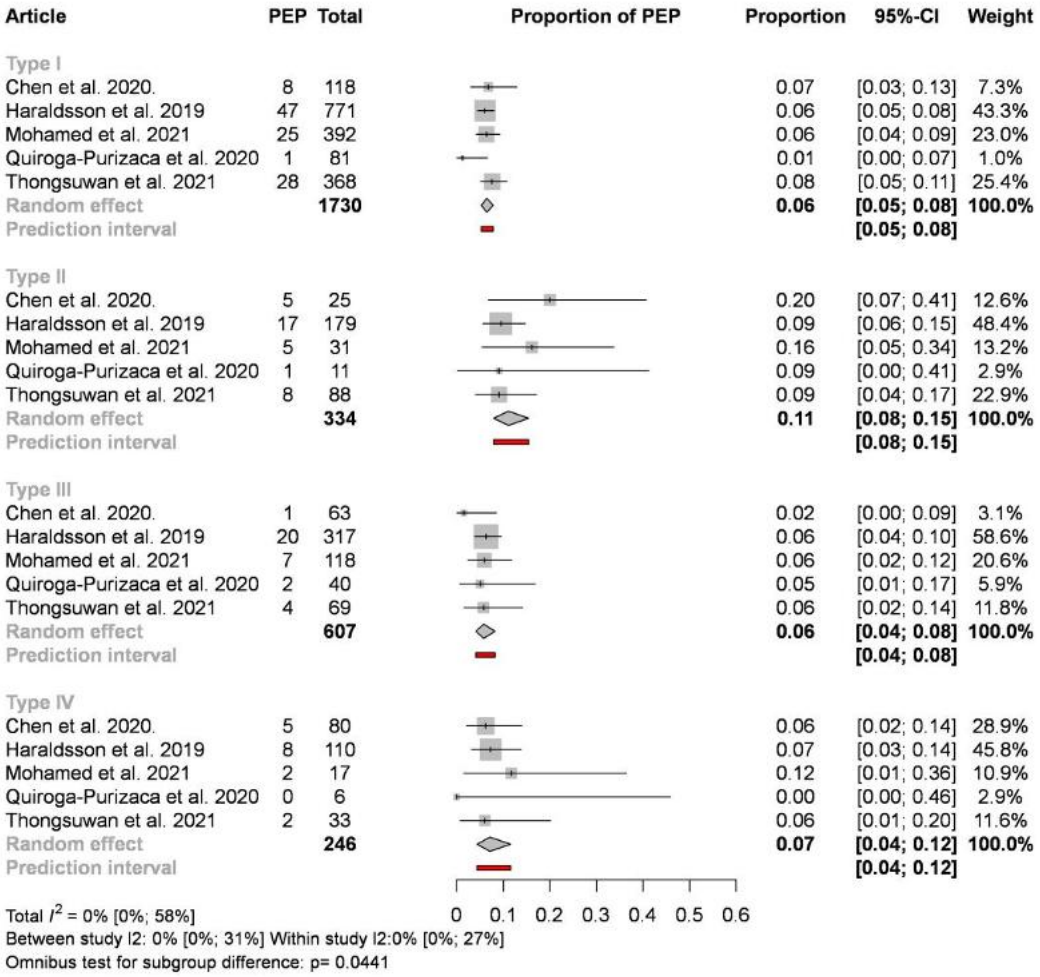


Figure 6. *Forest plot representing the pooled event rate of post-ERCP pancreatitis in the different papilla types in studies using the Haraldsson classification, showing a statistically significantly higher rate of post-ERCP pancreatitis in type II papilla, compared to the other papilla types (38). CI: confidence interval; PEP: post-ERCP pancreatitis.*

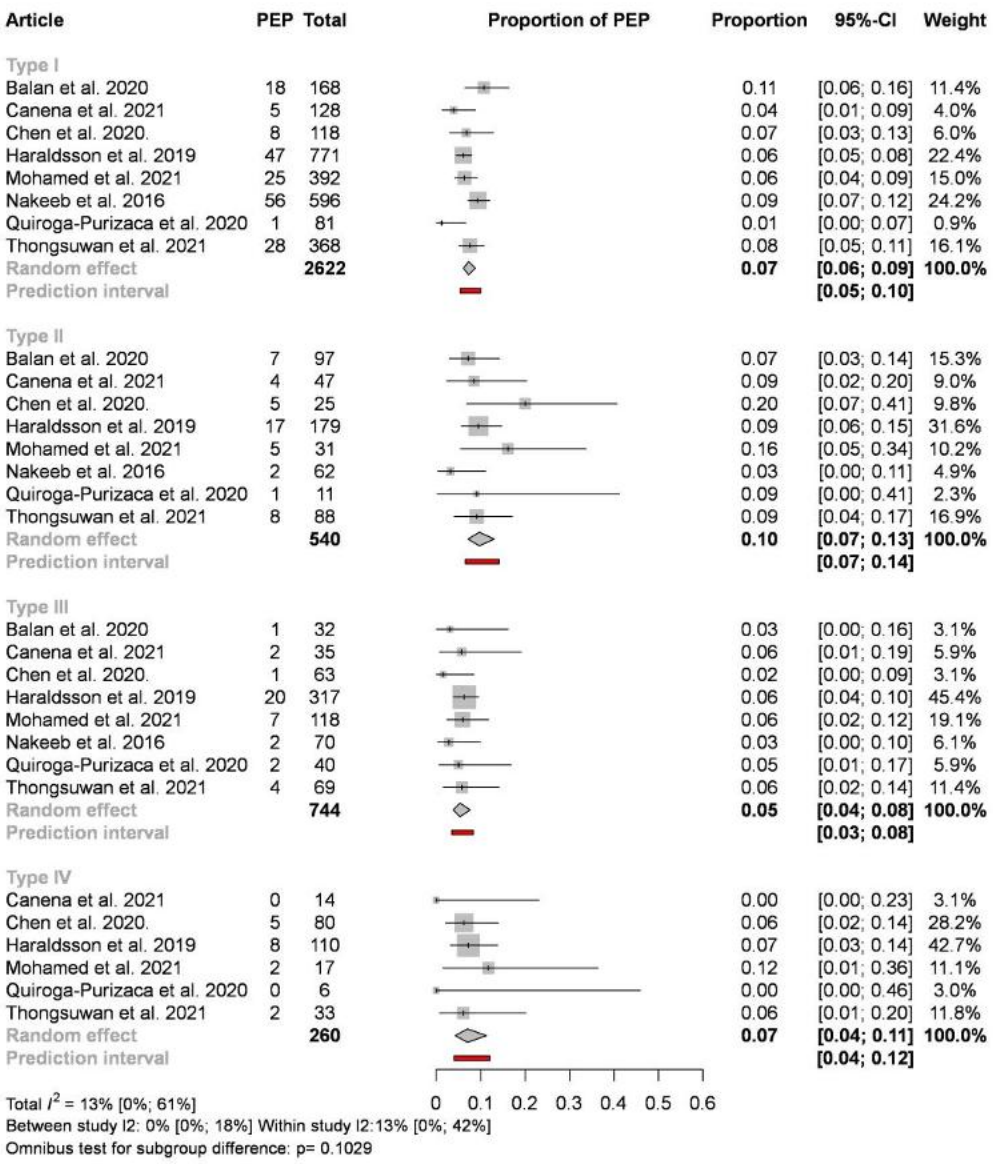


Figure 7. *Forest plot representing the pooled event rate of post-ERCP pancreatitis in the different papilla types in studies using different classification systems, showing a higher tendency for post-ERCP pancreatitis in type II papilla, compared to the other papilla types (38). CI: confidence interval; PEP: post-ERCP pancreatitis.*

8.1.3.4. Post-ERCP bleeding

Six studies provided data on post-ERCP bleeding and all of them applied the Haraldsson classification or a comparable system (3, 23, 24, 28, 31, 34). When the analysis was restricted to studies using the Haraldsson classification, as well as when the different classifications were pooled, no significant differences were detected in bleeding rates across papilla types (p =

0.8585 and p = 0.8078, respectively; see Figures 8 and 9). Sensitivity analyses did not identify any influential outliers or relevant changes in the effect estimates.

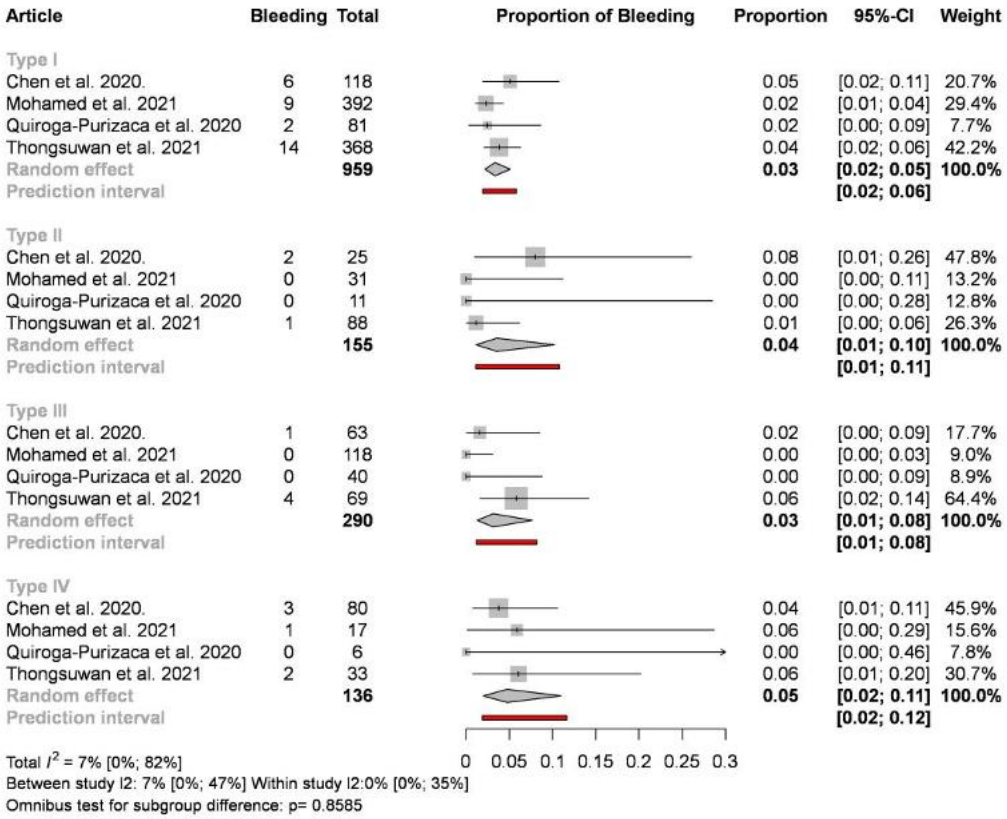


Figure 8. *Forest plot representing the pooled event rate of post-ERCP bleeding in the different papilla types in studies using the Haraldsson classification, showing no statistically significant difference in the event rates between the papilla types (38). CI: confidence interval.*

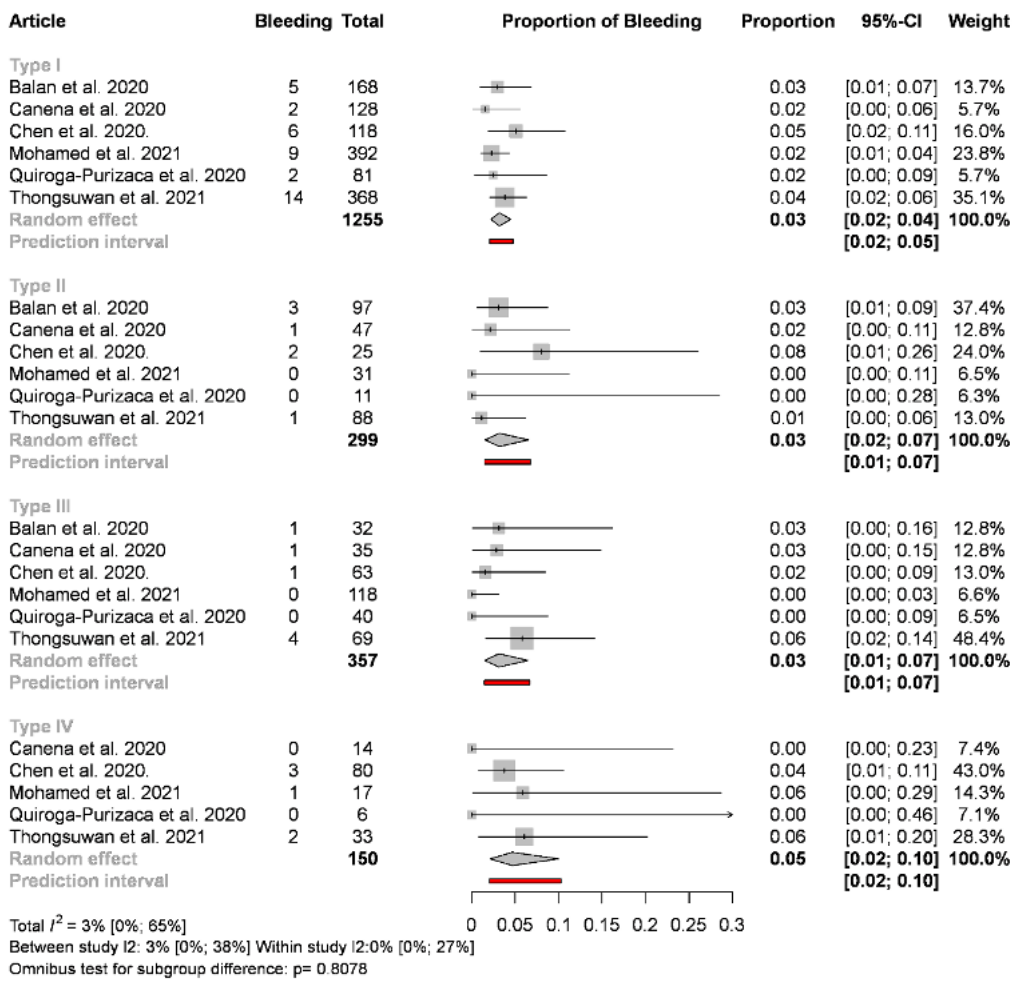


Figure 9. *Forest plot representing the pooled event rate of post-ERCP bleeding in the different papilla types in studies using different classification systems, showing no statistically significant difference in the event rate between the papilla types (38). CI: confidence interval.*

8.1.4. Qualitative synthesis

8.1.4.1. Cannulation time

Eight studies assessed cannulation time in relation to papilla morphology (3, 4, 23-25, 28, 31, 36), four of which applied the Haraldsson classification (3, 4, 28, 31). Across all studies, type I papillae were associated with the shortest cannulation times. Two studies reported the longest cannulation times in type II papillae (3, 4), while another two studies found the highest values in type IV papillae (28, 31).

8.1.4.2. Cannulation attempts

Four studies examined the number of cannulation attempts in relation to papilla morphology (23, 28, 31, 35), of which two applied the Haraldsson classification (28, 31). Across these analyses, cannulation attempts were consistently highest in type IV papillae, whereas the lowest numbers were reported for type I and type III papillae.

8.1.4.3. Post‑ERCP perforation

Three studies evaluated the rate of perforation following ERCP, all applying the Haraldsson classification (3, 24, 31). Meta-analysis could not be performed due to the presence of zero events across the studies.

8.1.4.4. Post‑ERCP infection

Four studies reported on post-ERCP infectious complications (3, 23, 28, 34), with three of these studies applying the Haraldsson classification (3, 28, 34). In the study by Chen et al., cholangitis occurred most frequently in type I papillae (2.5%), while no events were observed in type II or type III papillae (3). By contrast, Mohamed et al. found the highest rate of cholangitis and/or sepsis in type II papillae (3.2%), with no reported events in types III and IV (28). In the study of Thongsuwan et al., infections were most frequent in type III papillae (10.5%) and least frequent in type I papillae (6%) (34).

8.1.5. Risk of Bias and Quality of Evidence Assessment

The majority of the included studies showed a low risk of bias according to the applied assessment criteria across the reported outcomes. In addition, the conducted analyses did not indicate the presence of publication bias.

As only observational cohort studies were available, the certainty of evidence was limited and ranged from very low to low across the evaluated outcomes.

8.2. Study 2: At admission hemodynamic instability is associated with increased mortality and rebleeding rate in acute gastrointestinal bleeding: a systematic review and meta-analysis

8.2.1. Study search and selection

A total of 11,583 records were retrieved through the database search. After removing duplicates and screening titles and abstracts, 218 articles were selected for full-text review. An additional three studies were identified through reference screening and manual searches. In the end, 62 studies were included in the qualitative synthesis (39-100), of which 39 were eligible for quantitative analysis (40-48, 50, 52-54, 56-59, 63-67, 69, 72, 74, 76, 80, 82, 84, 86, 87, 92, 93, 95-100). The full study selection process is presented in the PRISMA flow diagram (see Figure 10).

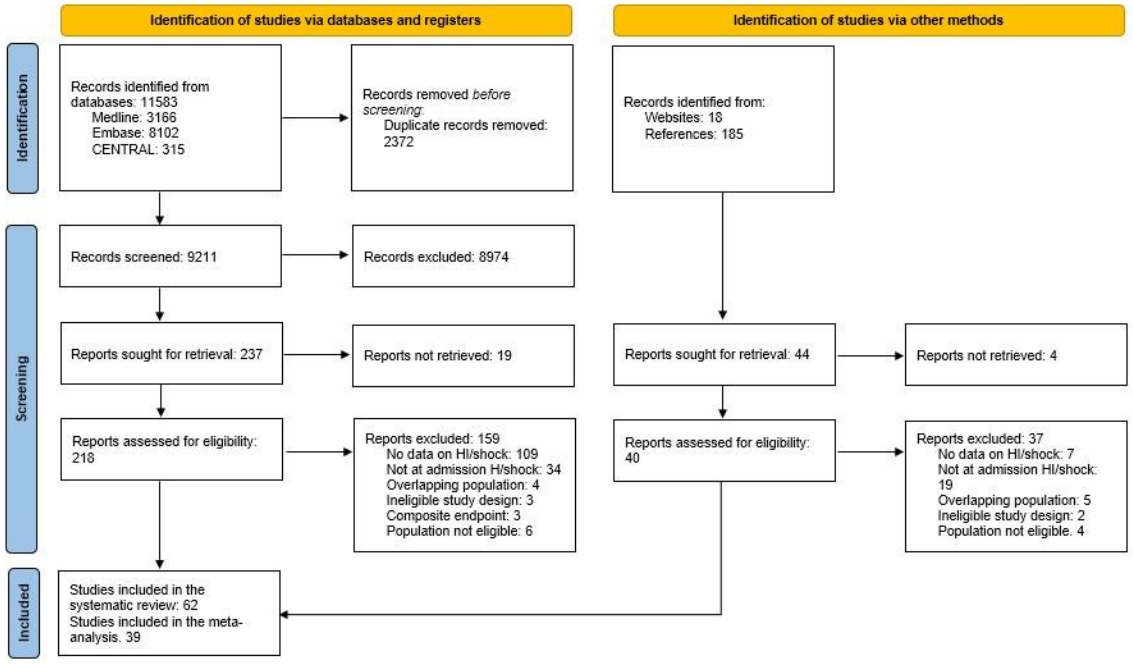


Figure 10. *PRISMA 2020 flowchart representing the detailed systematic search and study selection process (101).*

8.2.2. Basic characteristics of included studies

The main characteristics of the included studies are summarized in Table 2. The eligible publications were published between 1977 and 2021, and the number of participants per study ranged from 56 to 12,601. Most of the identified studies followed a cohort design, including 23 prospective (40-42, 44, 45, 48, 52, 53, 55, 56, 59, 64, 65, 67, 72, 74, 75, 78, 80, 84, 88, 94, 98) and 32 retrospective investigations (39, 43, 46-51, 54, 58, 60, 63, 66, 68-71, 73, 76, 82, 83, 85-

87, 89-93, 95-97, 99), while two were conducted in an ambidirectional manner (57, 100). In addition, the review comprised one randomized controlled trial (79), one case–control study (77), and three cross-sectional studies (61, 62, 81).

The reported proportion of patients with HI or shock varied widely across the studies, ranging from 1.2% to 68.3%. In terms of bleeding source, 54 studies focused on UGIB (40-59, 61-69, 71-82, 84, 86, 87, 89, 92-100), while 7 studies investigated LGIB (39, 60, 70, 85, 88, 90, 91), and one study included both patient groups within the same population (83).

Regarding outcomes, 44 studies reported mortality (40, 42-45, 47, 49-53, 55-57, 59, 61-68, 71-74, 76, 78-82, 84, 86, 88, 92-96, 98-100), 27 studies examined rebleeding (39, 41-43, 45, 46, 48, 51, 56, 58, 60, 67, 69, 70, 72, 74, 75, 77, 79, 81-85, 88, 89, 100), and 5 studies assessed the need for surgical intervention (39, 54, 87, 90, 97). Furthermore, two studies provided data on transfusion requirements (72, 89), and another two studies reported information on the length of hospitalization (39, 91).

Table 2. Basic characteristics of the included articles in Study 2 (101).

Author	Year	Study type	Type of bleeding	N⁰ of patients	Shock/HI (%)	Outcomes	Results
Albeldawi et al. (39)	2014	retrospective cohort	LGIB	56	51.8%	in-hospital rebleeding need for surgery length of hospitalization	HR: 3.80 (CI: 1.06–13.70) HR: 13.5 (CI: 3.2–56.5) HR: 1.1 (CI: 1.05–1.2)
Ardevol et al. (40)	2017	prospective cohort	UGIB	790	27.3%	6-week mortality	OR: 2.82 (CI: 1.94–4.09)
Bornman et al. (41)	1985	prospective cohort	PUB	177	14.5%	in-hospital rebleeding	OR: 14.67 (CI: 5.21–41.25)
Branicki et al. (42)	1992	prospective cohort	PUB	842	17.5%	in-hospital mortality in-hospital rebleeding	OR: 1.96 (CI: 0.92–4.17) OR: 1.60 (CI: 1.01–2.52)
Bratanic et al. (43)	2013	retrospective cohort	PUB	251	1.2%	in-hospital mortality in-hospital rebleeding	OR: 29.00 (CI: 2.49–337.18) OR: 13.50 (CI: 1.19–153.19)
Brullet et al. (44)	1996	prospective cohort	PUB	106	23.6%	in-hospital mortality	OR: 3.34 (CI: 1.00–11.10)
Budimir et al. (45)	2017	prospective cohort	PUB	796	9.7%	30-day mortality in-hospital rebleeding	OR: 5.56 (CI: 2.75–11.24) OR: 12.81 (CI: 7.28–22.53)
Bunchorntavakul et al. (46)	2017	retrospective cohort	NVUGIB VUGIB	180 106	8.3% 16%	30-day rebleeding	OR: 10.65 (CI: 3.57–31.78) OR: 1.99 (CI: 0.37–10.65)
Chaabane et al. (47)	2011	retrospective cohort	UGIB	401	9.5%	in-hospital mortality	OR: 19.70 (CI: 6.43–60.32)
Chandnani et al. (48)	2019	prospective cohort	UGIB	300	35.3%	30-day rebleeding	OR: 2.54 (CI: 1.37–4.71)
Charatcharoenwitthaya et al. (49)	2011	retrospective cohort	UGIB	526	59.5%	30-day mortality	HR: 2.57 (CI: 1.05–7.76)
Cheng et al. (50)	2014	retrospective cohort	PUB	785	12.9%	in-hospital mortality	OR: 5.66 (CI: 2.86–11.21)
Chirapongsathorn et al. (51)	2021	retrospective cohort	VUGIB	713	72.5%	5-day mortality 6-week mortality 5-day rebleeding 6-week rebleeding	HR: 12.25 (CI: 7.09–21.16) HR: 12.91 (CI: 7.95–20.97) HR: 2.32 (CI: 1.30–4.15) HR:2.14 (CI: 1.27–3.64)
Chiu et al. (52)	2009	prospective cohort	PUB	3220	20%	in-hospital mortality	OR: 2.85 (CI: 2.15–3.77)
Clason et al. (53)	1986	prospective cohort	UGIB	326	18%	in-hospital mortality	OR: 9.33 (CI. 4.49–19.37)
Danne et al. (54)	1984	retrospective cohort	UGIB	153	22.9%	need for surgery	OR: 3.23 (CI: 1.27–8.21)
Del Piano et al. (55)	2013	prospective cohort	NVUGIB	1413	9.3%	in-hospital mortality	OR: 2.89 (CI: 0.93–8.94)
Djuranovic et al. (56)	2007	prospective cohort	NVUGIB	315	21.6%	in-hospital mortality in-hospital rebleeding	OR: 18.69 (CI: 3.93–88.78) OR: 2.43 (CI: 1.28–4.61)
Elloumi et al. (58)	2003	retrospective cohort	PUB	208	6.7%	in-hospital rebleeding	OR: 3.91 (CI: 1.11–13.75)

El Mekkaoui et al. (57)	2011	ambidirectional cohort	UGIB	1303	2%	in-hospital mortality	OR: 5.60 (CI: 2.29–13.72)
Elsebaey et al. (59)	2018	prospective cohort	UGIB	286	56.6%	in-hospital mortality	OR: 4.47 (CI: 1.49–13.38)
Fujino et al. (60)	2013	retrospective cohort	LGIB	90	41.1%	30-day rebleeding	OR: 5.56 (CI: 2.00–15.57)
Gado et al. (62)	2014	cross-sectional	PUB	62	48.4%	2-week mortality	OR: 1.67 (CI: 0.26–10.74)
Gado et al. (61)	2014	cross-sectional	VUGIB	224	17.4%	2-week mortality	OR: 4.08 (CI: 1.52–10.96)
Hassanien et al. (63)	2018	retrospective cohort	VUGIB	725	28.7%	in-hospital mortality	OR: 7.69 (CI: 5.29–11.17)
Hunt et al. (64)	1983	prospective cohort	PUB	633	29.1%	in-hospital mortality	OR: 14.96 (CI: 6.12–36.55)
Hwang et al. (65)	2016	prospective cohort	NVUGIB	1584	9.8%	30-day mortality	OR: 2.75 (CI: 1.42–5.34)
Ishikawa et al. (66)	1995	retrospective cohort	PUB	75	56%	in-hospital mortality	OR: 11.93 (CI: 0.65–219.99)
Katschinski et al. (67)	1994	prospective cohort	UGIB	2217	NA	in-hospital mortality in-hospital rebleeding	OR: 4.40 (CI: 3.06–6.33) OR: 4.60 (CI: 3.90–5.43)
Kim et al. (69)	2005	retrospective cohort	M-W syndrome	159	22.6%	30-day rebleeding	OR: 6.37 (CI: 2.22–18.31)
Kim et al. (68)	2021	retrospective cohort	VUGIB	1373	6.3%	6-week mortality	HR: 4.43 (CI: 3.19–7.60)
Kitagawa et al. (70)	2019	retrospective cohort	LGIB	144	9%	90-day rebleeding	OR: 6.20 (CI: 1.75–21.97)
Koch et al. (71)	2013	retrospective cohort	UGIB	463	NA	in-hospital mortality	OR: 4.26 (CI: 1.11–16.3)
Lakatos et al. (72)	2021	prospective cohort	NVUGIB	688	NA	in-hospital mortality in-hospital rebleeding need for transfusion	OR: 1.80 (CI: 1.11–2.92) OR: 2.15 (CI: 1.33–3.47)
Lanas et al. (73)	2013	retrospective cohort	PUB	539	6.7%	30-day mortality	OR: 4.36 (CI: 0.02–6.09)
Laursen et al. (74)	2017	prospective cohort	PUB	12601 6643	23.3% 22.7%	in-hospital mortality in-hospital rebleeding 30-day mortality	OR: 3.60 (CI: 3.09–4.18) OR: 2.12 (CI: 1.91–2.36) OR: 2.95 (CI: 2.48–3.51)
Lausevic et al. (75)	2007	case-control	PUB	80	30%	in-hospital rebleeding	OR: 52.76 (CI: 6.58–423.02)
Lee et al. (76)	1992	retrospective cohort	VUGIB	101	56.7%	in-hospital mortality	OR: 2.28 (CI: 1.01–5.16)
Liang et al. (77)	2012	retrospective case-control	PUB	413	52.8%	30-day rebleeding	OR: 1.42 (CI: 0.88–2.28)
Lohse et al. (78)	2015	prospective cohort	PUB	3580	25.7%	90-day mortality	OR: 2.03 (CI: 1.69–2.43)
Mäkelä et al. (79)	1996	RCT	PUB	78	19.2%	30-day mortality	OR: 11.09 (CI:1.80–68.10)
Marmo et al. (80)	2014	prospective cohort	NVUGIB	2317	7%	30-day mortality	OR: 5.52 (CI: 3.47–8.79)
Minakari et al. (81)	2017	retrospective cross-sectional	UGIB	4747	39.8%	in-hospital mortality in-hospital rebleeding	OR: 39.84 (CI: 21.71–73.09) OR: 3.50 (CI: 2.98–4.10)

Mungan et al. (82)	2012	retrospective cohort	NVUGIB	423	NA	30-day mortality 30-day rebleeding	OR: 7.28 (CI: 1.81–29.24) OR: 3.49 (CI: 1.13–10.80)
Nagata et al. (83)	2017	retrospective cohort	GIB	157	20.4%	90-day rebleeding	OR: 2.90 (CI: 1.10–7.70)
Nahon et al. (84)	2012	prospective cohort	UGIB	3298	7.7%	in-hospital mortality in-hospital rebleeding	OR: 4.24 (CI: 3.07–5.85)
Nykänen et al. (85)	2018	retrospective cohort	LGIB	NA	NA	30-day rebleeding	OR: 0.59 (CI: 0.17–2.06)
Ogasawara et al. (86)	2014	retrospective cohort	PUB	428	10.3%	in-hospital mortality	OR: 13.98 (CI: 2.27–86.08)
Parreira et al. (87)	2002	retrospective cohort	PUB	200	13.5%	need for surgery	OR: 3.86 (CI: 1.47–10.15)
Radaelli et al. (88)	2021	prospective cohort	LGIB	1198	9.2%	in-hospital mortality in-hospital rebleeding	OR: 5.07 (CI: 2.54–10.11) OR: 1.85 (CI: 1.01–3.42)
Restellini et al. (89)	2012	retrospective cohort	NVUGIB	1677	31.9%	in-hospital rebleeding need for transfusion	OR: 1.10 (CI: 0.80–1.50) OR: 3.42 (CI: 2.73–4.28)
Rios et al. (90)	2007	retrospective cohort	LGIB	171	17%	need for surgery	OR: 4.81 (CI: 1.87–12.37)
Schmulewitz et al. (91)	2003	retrospective cohort	LGIB	565	68.3%	length of hospitalization	HR: 0.80 (CI: 0.70–1.00)
Sereda et al. (92)	1977	retrospective cohort	UGIB	513	24.2%	in-hospital mortality	OR: 8.93 (CI: 4.57–17.46)
Shih et al. (93)	2018	retrospective cohort	UGIB	202	22.3%	in-hospital mortality	OR: 7.60 (CI: 2.40–24.05)
Sombié et al. (94)	2015	prospective cohort	UGIB	265	33.6%	30-day mortality	OR: 4.80 (CI: 1.90–11.70)
Stupin et al. (95)	2013	retrospective cohort	PUB	895	28.4%	30-day mortality	OR: 6.80 (CI: 4.87–9.49)
Thomopoulos et al. (97)	2004	retrospective cohort	PUB	191	16.8%	need for surgery	OR: 3.85 (CI: 1.68–8.81)
Thomopoulos et al. (96)	2006	retrospective cohort	VUGIB	141	18.4%	6-week mortality 1-year mortality	OR: 6.18 (CI: 2.39–16.03) OR: 1.70 (CI: 0.70–4.06)
Tsoi et al. (98)	2002	prospective cohort	PUB	8222	8.7%	30-day mortality	OR: 3.62 (CI: 2.77–4.70)
Vuachet et al. (99)	2015	retrospective cohort	VUGIB	121 112	11.6% 10.7%	6-week mortality 6-month mortality 6-month rebleeding	OR: 4.60 (CI: 1.40–15.13) OR: 3.42 (CI: 1.09–10.70) OR: 3. 76 (CI: 1.09–12.86)
Wierchowski et al. (100)	2013	ambidirectional cohort	NVUGIB	482	19.3%	in-hospital mortality in-hospital rebleeding	OR: 11.50 (CI: 5.43–24.36) OR: 3.30 (CI: 1.91–5.72)

LGIB: lower gastrointestinal bleeding; UGIB: upper gastrointestinal bleeding; PUB: peptic ulcer bleeding; NVUGIB: non-variceal upper gastrointestinal bleeding; VUGIB: variceal upper gastrointestinal bleeding; M-W: Mallory-Weiss; NA: not available; HR: hazard ratio; OR: odds ratio

8.2.3. Mortality

8.2.3.1. In-hospital mortality

A total of 27 studies assessed the association between HI and in-hospital mortality in UGIB (42-44, 47, 50-53, 55-57, 59, 63, 64, 66, 67, 71, 72, 76, 81, 84, 86, 88, 92, 93, 100, 102), of which 22 provided sufficient data to be included in the meta-analysis (42-44, 47, 50, 52, 53, 56, 57, 59, 63, 64, 66, 67, 72, 76, 84, 86, 92, 93, 100, 102). The pooled results demonstrated a significantly increased odds of in-hospital mortality among patients presenting with HI (OR: 5.48; CI: 3.99–7.52; I^2 = 74%) (see Figure 11). Subgroup analyses were conducted for overall UGIB, non-variceal UGIB (NVUGIB), and PUB (peptic ulcer bleeding). In studies including all UGIB cases, the odds of in-hospital mortality were higher (OR: 6.18; CI: 4.11–9.28) compared with studies restricted to PUB patients (OR: 4.79; CI: 2.62–8.97). In the NVUGIB subgroup, the association did not reach statistical significance (OR: 6.52; CI: 0.29–144.21). Influence analysis did not identify any outlying study that would have substantially affected the pooled estimate.

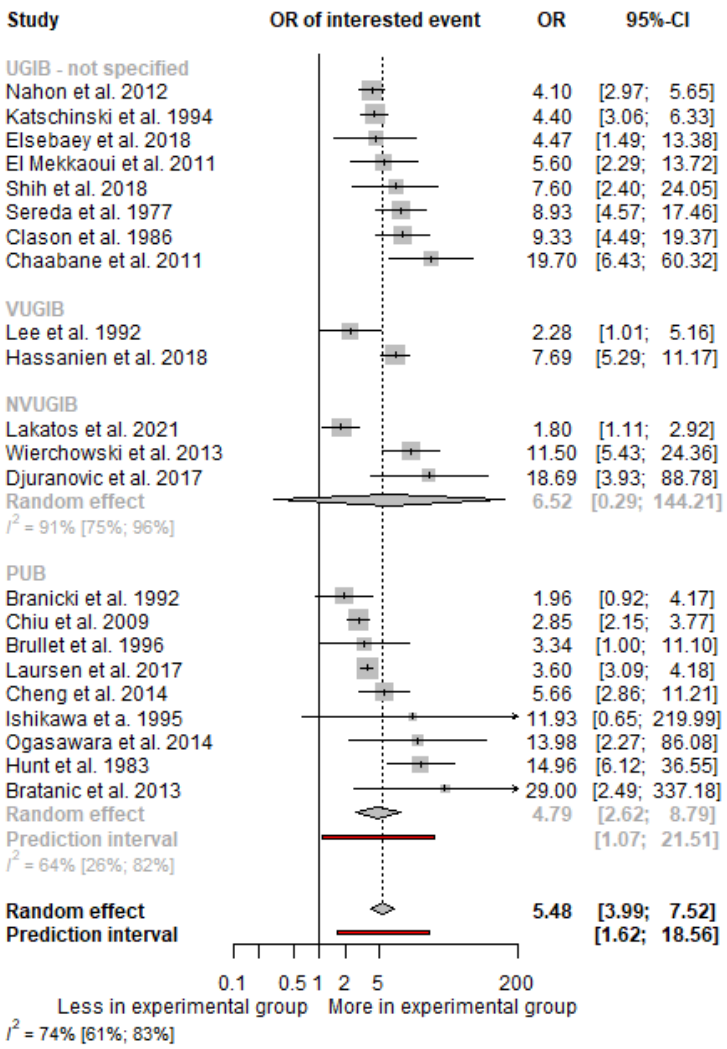


Figure 11. *Forest plot representing the odds of in-hospital mortality in patients with upper gastrointestinal bleeding, demonstrating a substantially higher odds of death in the presence of hemodynamic instability. NVUGIB: non-variceal upper gastrointestinal bleeding; PUB: peptic ulcer bleeding; UGIB: upper gastrointestinal bleeding; VUGIB: variceal upper gastrointestinal bleeding; OR: odds ratio; CI: confidence interval (101).*

In the subgroup of studies defining HI as a systolic blood pressure ≤ 100 mmHg and/or a pulse rate ≥ 100/min, the odds of in-hospital mortality remained significantly increased, although at a lower magnitude (OR: 4.14; CI: 2.47–6.94; $I^2 = 67\%$) (see Figure 12).

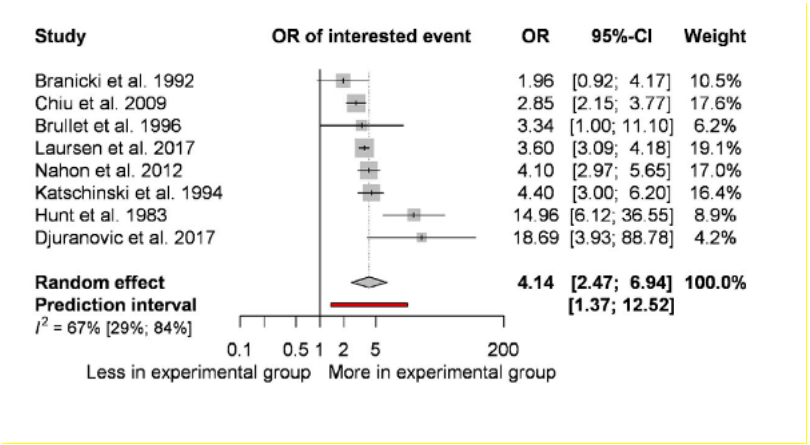


Figure 12. *Forest plot representing the odds of in-hospital mortality in upper gastrointestinal bleeding in studies defining hemodynamic instability as a systolic blood pressure ≤ 100 mmHg and/or a pulse rate ≥ 100/min, demonstrating a significantly increased odds of death in the presence of hemodynamic instability. OR: odds ratio; CI: confidence interval (101).*

In addition to the studies included in the meta-analysis, four cohort studies and one cross-sectional study — which could not be pooled quantitatively — likewise reported higher odds of in-hospital mortality among UGIB patients presenting with HI (51, 55, 71, 81, 88).

Furthermore, one study that examined a mixed cohort of patients with UGIB and LGIB, also demonstrated increased odds of in-hospital mortality in hemodynamically unstable patients (OR: 5.07; CI: 2.54–10.11) (83).

8.2.3.2. Follow-up mortality

A total of 19 studies evaluated follow-up mortality, all involving patients with UGIB (40, 45, 49, 51, 61, 62, 65, 68, 73, 74, 78-80, 82, 94-96, 98, 99). Of these, 16 reported outcomes at 30–42 days (40, 45, 49, 51, 65, 69, 73, 74, 79, 80, 82, 94-96, 98, 99), and 10 provided sufficient data to be included in the meta-analysis (40, 45, 65, 74, 80, 82, 95, 96, 98, 99). The pooled analysis demonstrated increased odds of mortality during the follow-up period (OR: 4.15; CI: 3.18–5.42; I^2 = 68%) (see Figure 13). Influence analysis did not identify any outlying study that would have substantially altered the pooled estimate.

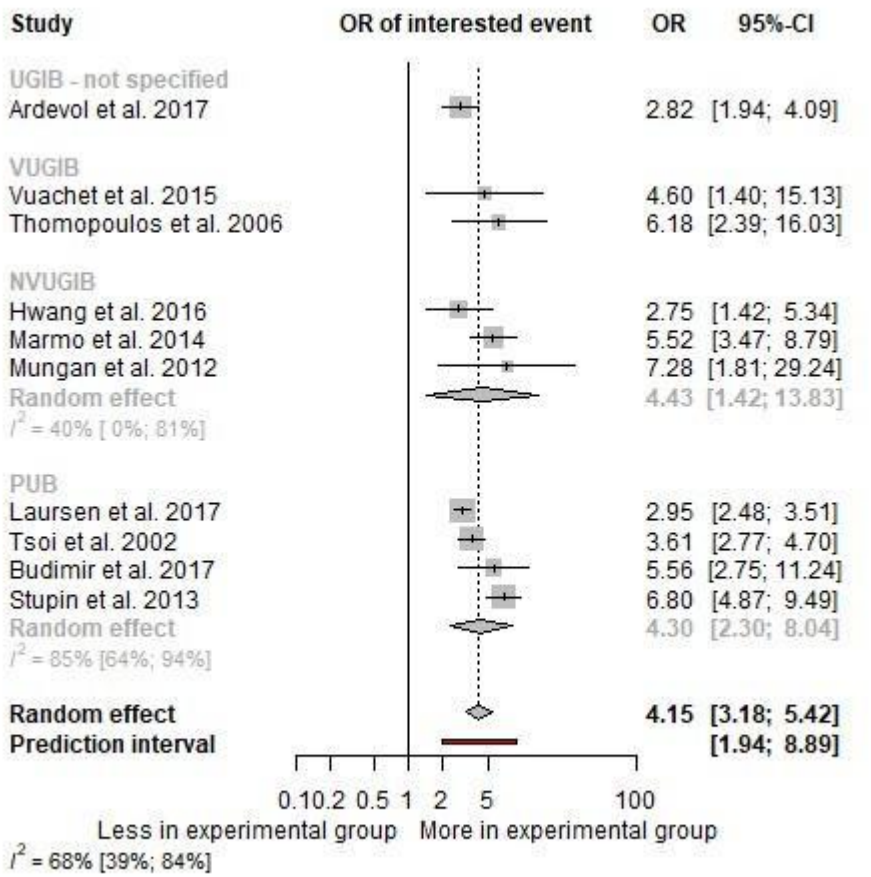


Figure 13. *Forest plot illustrating the odds of 30–42-day mortality in upper gastrointestinal bleeding, demonstrating a significantly increased odds of death during the follow-up period among patients presenting with hemodynamic instability. NVUGIB: non-variceal upper gastrointestinal bleeding; PUB: peptic ulcer bleeding; UGIB: upper gastrointestinal bleeding; VUGIB: variceal upper gastrointestinal bleeding; OR: odds ratio; CI: confidence interval (101).*

In the subgroup of studies defining HI as a systolic blood pressure ≤ 100 mmHg and/or a pulse rate ≥ 100/min, the association with 30–42-day mortality remained statistically significant (OR: 4.03; CI: 2.68–6.05; $I^2 = 58\%$) (see Figure 14).

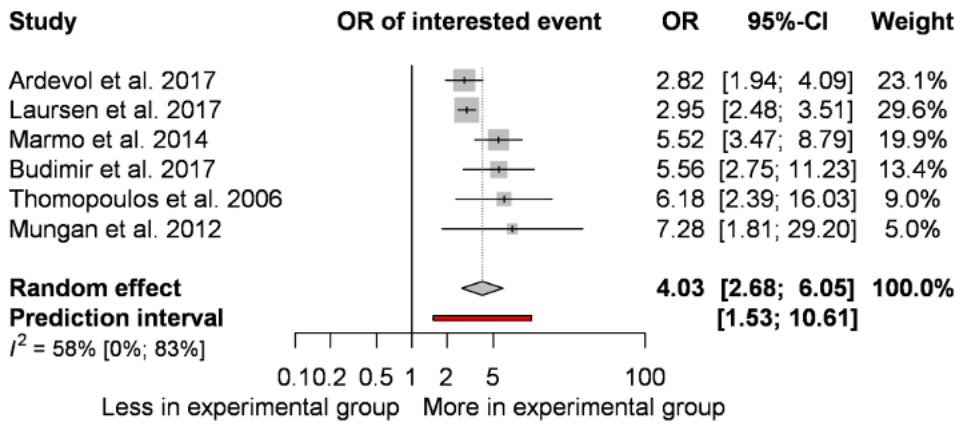


Figure 14. *Forest plot illustrating the odds of 30–42-day mortality in upper gastrointestinal bleeding among studies that defined hemodynamic instability as a systolic blood pressure ≤ 100 mmHg and/or a pulse rate ≥ 100/min, demonstrating an increased odds of mortality in patients presenting with hemodynamic instability. OR: odds ratio; CI: confidence interval (101).*

In addition, six further eligible studies — five cohort studies and one randomized controlled trial — also reported increased mortality among patients with HI (49, 51, 68, 73, 79, 94).

Two studies assessed 2-week mortality, one in PUB and one in variceal UGIB (VUGIB). In the VUGIB population, HI was associated with a higher odds of 2-week mortality (OR: 4.08; CI: 1.52–10.96), whereas in PUB the association did not reach statistical significance (OR: 1.67; CI: 0.26–10.74) (61, 62).

Furthermore, Lohse et al. reported an increased odds of 90-day mortality in PUB patients with HI (OR: 2.03; CI: 1.69–2.43) (78).

8.2.4. Rebleeding

8.2.4.1. In-hospital rebleeding

In total, 17 studies investigated the association between in-hospital rebleeding and HI, of which 15 focused on UGIB and 2 on LGIB (39, 41-43, 45, 51, 56, 58, 67, 72, 74, 75, 81, 84, 88, 89, 100). Among the studies with UGIB as the bleeding source, 11 were included

in the meta-analysis (41-43, 45, 56, 58, 67, 72, 74, 84, 100). Our findings demonstrated higher odds of in-hospital rebleeding in the presence of HI in UGIB (OR 3.68; CI 2.24–6.50; I^2 = 91%) (see Figure 15). Subgroup analyses were conducted for NVUGIB and PUB, showing that the odds were higher in PUB patients compared with those with NVUGIB (OR 4.95; CI 1.70–14.44 vs. OR 2.55; CI 1.44–4.50). The influence analysis identified the study by Budimir et al. as an outlier; however, no clinical explanation could be determined for this finding (45).

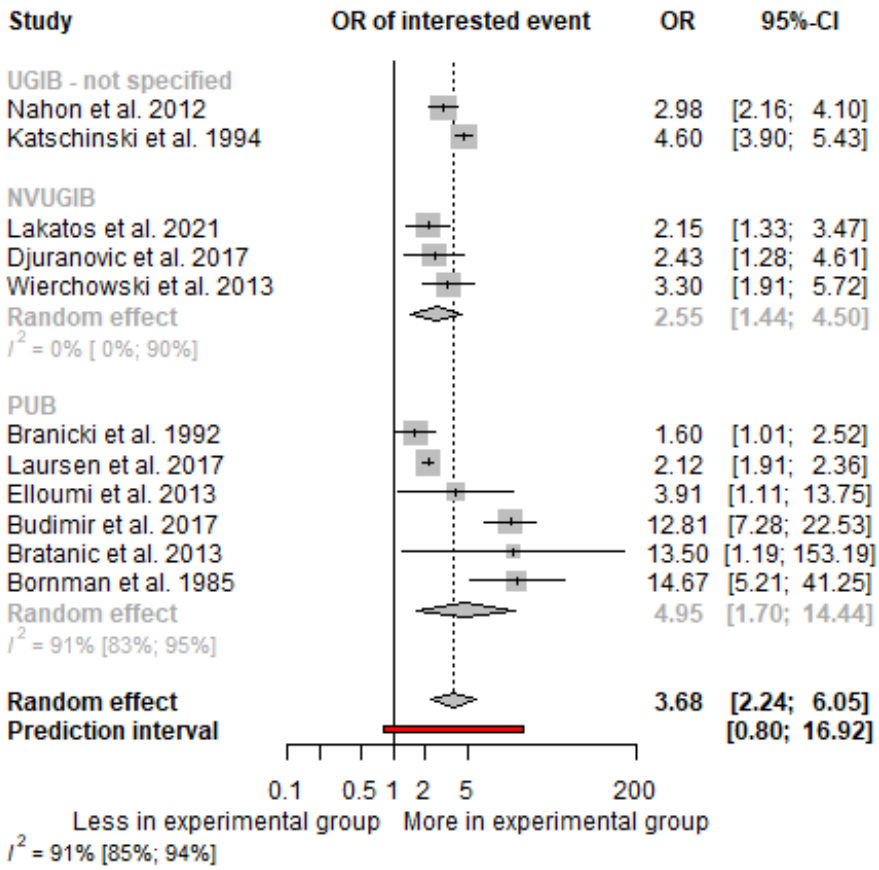


Figure 15. *Forest plot representing the odds of in-hospital rebleeding in patients with UGIB, demonstrating an increased odds of rebleeding in the presence of hemodynamic instability. Subgroup analyses indicated higher odds among patients with PUB compared with those with NVUGIB. NVUGIB: non-variceal upper gastrointestinal bleeding; PUB: peptic ulcer bleeding; UGIB: upper gastrointestinal bleeding; VUGIB: variceal upper gastrointestinal bleeding; OR: odds ratio; CI: confidence interval (101).*

In the subgroup of studies defining HI as a systolic blood pressure ≤100 mmHg and/or a pulse rate ≥100/min, significantly increased, although comparatively lower, odds of in-hospital rebleeding were observed in unstable patients (OR 3.92; CI 1.80–8.55; $I^2 = 94\%$) (see Figure 16).

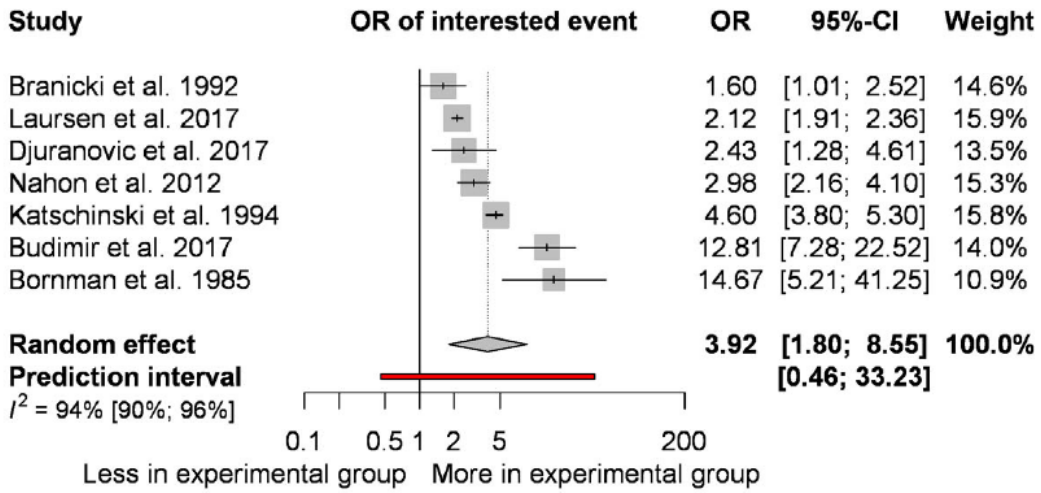


Figure 16. *Forest plot representing the odds of in-hospital rebleeding in patients with upper gastrointestinal bleeding in studies defining hemodynamic instability as a systolic blood pressure ≤100 mmHg and/or a pulse rate ≥100/min, showing significantly increased odds of rebleeding in hemodynamically unstable patients. OR: odds ratio; CI: confidence interval (101).*

In addition, four studies that were not included in the meta-analysis also reported higher odds of in-hospital rebleeding (51, 75, 81, 89). Two further studies examining hemodynamically unstable patients with LGIB likewise demonstrated increased rebleeding risk (HR 3.78; CI 1.06–13.7; OR 1.85; CI 1.01–3.42) (39, 88).

8.2.4.2. Follow-up rebleeding

Eight studies evaluated the association between HI and 30-42-day rebleeding, seven in patients with UGIB and one in LGIB (46, 48, 51, 60, 69, 77, 82, 85). Four UGIB studies were eligible for inclusion in the meta-analysis, resulting in an odds ratio of 4.12 (CI 1.83–9.31; $I^2 = 39\%$) (see Figure 17). Due to the limited number of studies, the leave-one-out sensitivity analysis had restricted interpretability.

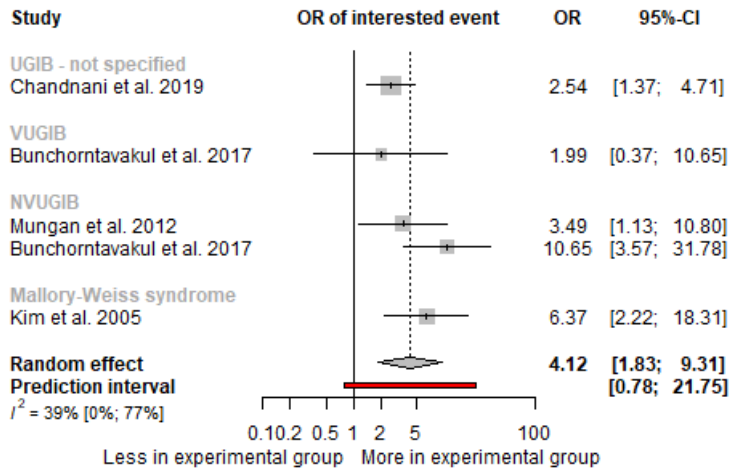


Figure 17. *Forest plot representing the odds of 30–42-day rebleeding in patients with upper gastrointestinal bleeding, showing increased odds in the presence of hemodynamic instability. VUGIB: variceal upper gastrointestinal bleeding; UGIB: upper gastrointestinal bleeding; NVUGIB: non-variceal upper gastrointestinal bleeding; OR: odds ratio; CI: confidence interval (101).*

In the subgroup of studies defining HI as a systolic blood pressure ≤100 mmHg and/or a pulse rate ≥100/min, comparable estimates were obtained (OR 5.44; CI 2.38–12.43; I^2 = 0%) (see Figure 18).

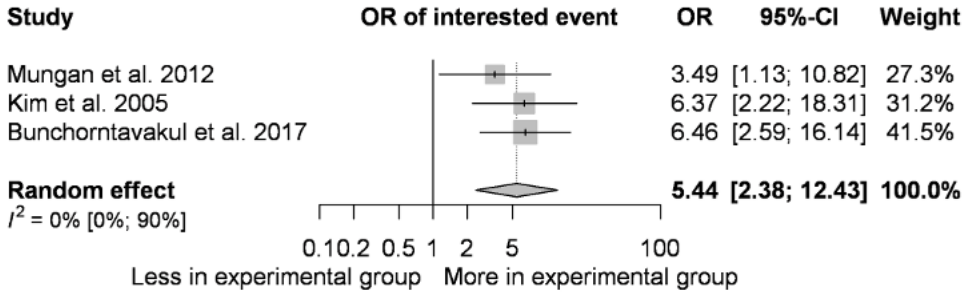


Figure 18. *Forest plot representing the odds of 30–42-day rebleeding in patients with upper gastrointestinal bleeding in studies defining hemodynamic instability as a systolic blood pressure ≤100 mmHg and/or a pulse rate ≥100/min, showing increased odds of rebleeding in hemodynamically unstable patients. OR: odds ratio; CI: confidence interval (101).*

The remaining four studies — three conducted in UGIB and one in LGIB — also demonstrated increased odds of 30- to 42-day rebleeding in case of HI (51, 60, 77, 85). Furthermore, two studies assessing 90-day rebleeding, one in LGIB and one in general GIB, similarly reported a higher odds of rebleeding among hemodynamically unstable patients (OR 6.20; CI 1.75–21.97; OR 2.90; CI 1.10–7.70) (70, 83).

8.2.5. Need for surgery

Five studies evaluated the requirement for surgical intervention in the context of HI. Among patients with UGIB, hemodynamic compromise was associated with an increased need to undergo surgery (OR 3.65; CI 2.17–6.14) (see Fig. 19) (54, 87, 97).

For LGIB, the two available studies similarly indicated an increased need for surgery in patients with HI (HR 13.5; CI 3.2–56.5 and OR 4.81; CI 1.87–12.37) (39, 90).

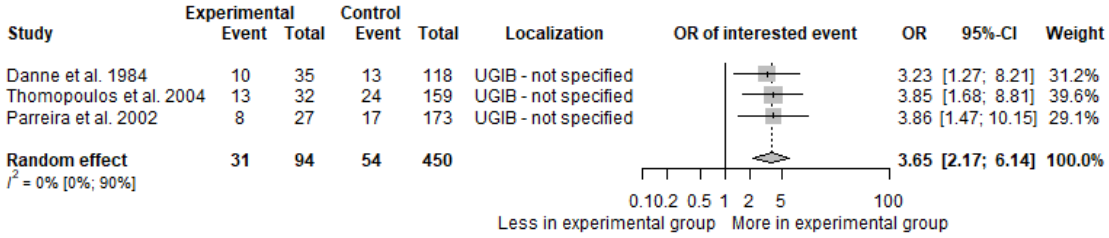


Figure 19. *Forest plot representing the odds of requiring surgery in patients with upper gastrointestinal bleeding, demonstrating a higher likelihood of surgical intervention in the presence of hemodynamic instability (101).*

8.2.6. Need for transfusion

Two studies reported on the need for blood transfusion. In both, the bleeding source was UGIB, and HI was associated with higher odds of requiring transfusion (OR 3.57; CI 2.6–5.0 and OR 3.42; CI 2.73–4.28) (72, 89).

8.2.7. Length of hospitalization

Two studies reporting on the length of hospitalization were identified, both involving patients with LGIB. Abeldawi et al. found that HI was associated with longer hospital stays (HR 1.1; CI 1.05–1.20) (39). In contrast, Schmulewitz et al. observed a tendency

toward shorter hospitalization in hemodynamically unstable patients (HR 0.8; CI 0.7–1.0), although this association did not reach statistical significance (91).

8.2.8. Need for endoscopic rescue therapy

We did not identify any studies that reported the use of endoscopic rescue therapy in hemodynamically unstable patients with GIB.

8.2.9. Risk of bias and publication bias assessment

Among the 27 studies reporting in-hospital mortality, one study (4%) was judged to have a high risk of bias, 13 (48%) a moderate risk, and 13 (48%) a low risk of bias. For follow-up mortality, two of the 19 studies (11%) were rated as high risk, eight (42%) as moderate risk, and nine (47%) as low risk. Of the 17 studies reporting in-hospital rebleeding, seven (42%) were classified as having a moderate risk of bias and ten (58%) as low risk. Regarding rebleeding during follow-up, three of the 11 studies (27%) were assessed as moderate risk, while eight (73%) were considered low risk. For the need for surgery, one of the five studies (20%) was categorized as low risk, whereas four (80%) were considered to have a moderate risk of bias. All four studies reporting on transfusion requirements and length of hospital stay were assessed as having a moderate risk of bias.

9. DISCUSSION

9.1. Summary of Findings, International Comparisons

Acute gastroenterological conditions often require urgent or semi-urgent diagnostic and therapeutic endoscopic interventions, in which procedural complexity and the risk of adverse events are determined by clinical factors and procedure-relevant anatomical characteristics identifiable at presentation. Early recognition of these factors is essential for procedural planning, appropriate allocation of expertise, and the implementation of risk-adapted preventive strategies, ultimately improving patient safety and clinically meaningful outcomes.

In this context, this PhD work synthesizes evidence from two systematic reviews and meta-analyses examining distinct but conceptually related risk factors in acute gastroenterological and endoscopic settings. Although the analyses address different clinical scenarios, both highlight the relevance of early, readily identifiable factors in guiding endoscopic management strategies. Collectively, these findings emphasize the role of risk stratification as an integral component of decision-making in acute gastrointestinal diseases.

The first systematic review and meta-analysis evaluated the role of papilla morphology in ERCP-related outcomes. Based on international data applying the Haraldsson classification, regular (type I) papillae were associated with a significantly lower rate of difficult cannulation, whereas type II papillae demonstrated an approximately twofold increased risk of post-ERCP pancreatitis. In contrast, no significant differences were observed between papilla types with respect to cannulation failure or post-ERCP bleeding. These findings are consistent with and extend results from previous international cohort studies, supporting papilla morphology as a relevant anatomical determinant of ERCP performance and safety.

The international literature has long debated the factors influencing ERCP success and safety, including patient-related characteristics, certain disease etiologies, and procedure-related variables (103). Within this framework, anatomical features of the papilla, including papilla morphology, have gained increasing attention as potential contributors to procedural complexity.

Several studies have explored the interaction between papilla type and endoscopist experience. Among the studies included in this analysis, the impact of endoscopist expertise on cannulation difficulty remains inconsistent. While some cohorts reported no clear association between difficult cannulation rates and operator experience, others observed higher rates of difficult cannulation and procedure-related adverse events in papilla types more frequently managed by less experienced endoscopists (4, 28). These observations are in line with broader evidence indicating that increasing endoscopist experience is associated with improved ERCP performance and safety (104, 105). These data suggest that papilla morphology should be considered both in procedural planning and in the context of endoscopic training.

In addition, international studies have reported differences in the use of rescue cannulation techniques across papilla morphologies. This variability may partly explain the absence of significant differences in cannulation failure rates between papilla types. Morphology-adapted strategies, such as needle-knife fistulotomy or precut sphincterotomy in regular papillae, transpancreatic sphincterotomy in small papillae, and needle-knife techniques in protruding or ridged papillae, have been proposed in the literature, supporting a more individualized approach to advanced biliary cannulation (106, 107).

Several papilla classification systems have been described in the literature; however, the Haraldsson classification remains the most widely used and well-recognized and therefore served as the basis of the present analysis. A key limitation of this classification is the lack of consideration of periampullary diverticulum (PAD). Recent data suggest that PAD may represent a distinct anatomical entity and is associated with an increased risk of cannulation failure and post-ERCP adverse events (28, 108). These observations indicate that classification systems incorporating PAD may allow a more comprehensive assessment of anatomical risk and should be considered in future studies and clinical practice.

The second systematic review and meta-analysis examined haemodynamic instability as a prognostic factor in acute GIB. Across a large international body of evidence, haemodynamic instability at presentation was consistently associated with a substantially increased risk of in-hospital and short-term mortality, rebleeding, and the need for

surgery, with the strongest associations observed in UGIB. These findings quantitatively confirm earlier observations from international cohort studies and further emphasize the prognostic relevance of early haemodynamic compromise in acute bleeding episodes.

In the international literature, haemodynamic instability has been defined heterogeneously, most commonly using systolic blood pressure and heart rate thresholds. Despite this variability, these parameters are universally and rapidly available in emergency settings and require no specialized equipment. The present meta-analysis demonstrates that abnormalities in these simple clinical markers at presentation are sufficient to identify patients at markedly increased risk of adverse outcomes. This observation is consistent with their incorporation into widely used pre-endoscopic risk scores, such as the Rockall and Glasgow–Blatchford scores, supporting their continued clinical relevance in early risk stratification (50, 109).

Importantly, the present findings indicate that haemodynamic parameters assessed at presentation alone are associated with an approximately fourfold increase in the odds of in-hospital mortality and rebleeding in acute GIB. This highlights the central prognostic role of early physiological assessment and supports the concept that haemodynamic instability represents a robust marker of disease severity, largely independent of subsequent therapeutic interventions.

From a clinical perspective, these results underscore the importance of prompt recognition, resuscitation, and stabilization of haemodynamically unstable patients presenting with acute GIB. Adequate early management may reduce the risk of severe adverse outcomes; however, several aspects of initial care remain insufficiently defined. In particular, uncertainty persists regarding the optimal rate and intensity of fluid resuscitation, the role of vasopressor therapy, and the most appropriate choice of resuscitation fluids, as reflected in current guideline recommendations (10).

The prognostic impact of haemodynamic instability also has important implications for the timing of endoscopy. Evidence from international studies indicates worse outcomes, including higher in-hospital mortality, when endoscopy is performed too early in inadequately stabilized patients, particularly in UGIB (102). In this context, current European guidelines emphasize the importance of adequate haemodynamic stabilization prior to endoscopic intervention (10). A plausible explanation is insufficient correction

of haemodynamic derangement before the procedure, potentially exacerbating circulatory compromise during endoscopy.

Overall, the findings of this work demonstrate that readily identifiable anatomical and physiological factors play a central role in risk stratification in acute gastroenterological conditions requiring endoscopic intervention. Papilla morphology represents a relevant anatomical determinant of ERCP complexity and procedure-related adverse events, whereas haemodynamic instability constitutes a strong prognostic marker of adverse outcomes in acute GIB. Recognition of these factors at presentation may support improved procedural planning, appropriate allocation of expertise, and more individualized, risk-adapted patient management in acute endoscopic practice.

9.2. Strengths

Both studies have several important strengths. Each addresses a clinically relevant yet previously underexplored risk factor in acute gastroenterological and endoscopic settings, providing quantitative evidence for its association with clinically meaningful outcomes.

A rigorous and transparent methodology was applied in both analyses. Comprehensive systematic searches were performed across multiple databases, study selection and data extraction were conducted according to predefined criteria, and appropriate meta-analytical methods were used. Between-study heterogeneity and potential sources of bias were systematically assessed, and sensitivity and subgroup analyses were performed where feasible.

In addition, both studies are based on a large body of evidence derived from diverse patient populations, enhancing the robustness and generalizability of the findings across different clinical contexts.

9.3. Limitations

Both studies have limitations that should be considered when interpreting the findings. First, in several analyses substantial between-study heterogeneity was observed. This likely reflects clinical and methodological differences across the included cohorts, such as variations in outcome definitions, procedural classifications and patient populations. Although standardized definitions were applied where feasible, definitions were not

uniform across studies, particularly for haemodynamic instability. This may have contributed to the observed heterogeneity.

Second, a considerable proportion of the included evidence originated from retrospective cohort studies. While these provide valuable real-world data, retrospective designs are inherently more susceptible to confounding, selection bias and incomplete reporting.

Third, for some outcomes the available evidence remained limited, and in certain analyses the risk of bias was moderate or high. Therefore, the results should be interpreted with appropriate caution.

Finally, variability in reporting and data granularity constrained the scope of some subgroup and sensitivity analyses.

Taken together, these limitations underline the need for prospective studies with more uniform definitions and more complete reporting.

10. CONCLUSIONS

10.1. Study 1

In conclusion, the morphology of the major papilla is associated with ERCP outcomes and procedure-related adverse events. Difficult cannulation occurred less frequently in type I papillae (26%) compared with other papilla types, whereas PEP was significantly more frequent in type II papillae (11%). In studies using the Haraldsson classification, no significant difference in cannulation failure rates was observed between papilla types.

10.2. Study 2

In conclusion, HI is strongly associated with worse clinical outcomes in patients with acute GIB. Hemodynamically compromised patients had increased odds of in-hospital mortality, with an approximately fivefold higher risk (OR 5.48; CI 3.99–7.52). In addition, HI was associated with higher odds of in-hospital rebleeding (OR 3.68; CI 2.24–6.50) and a higher need for surgical intervention in UGIB (OR 3.65; CI 2.84–4.68).

11. IMPLICATIONS FOR PRACTICE

11.1. Study 1

Based on our results, papilla morphology should be routinely assessed and documented prior to or at the start of ERCP. During the training of fellow endoscopists, procedures should initially be performed in patients with type I papillae, which are associated with the lowest rate of difficult cannulation.

In contrast, type II papillae, which are associated with the highest rates of PEP, should preferably be managed by more experienced endoscopists. Given the increased risk of PEP in this papilla type, these cases require particular caution, including careful cannulation strategies, strict adherence to prophylactic measures, and enhanced post-procedural monitoring, as well as thorough patient education regarding procedure-related adverse events.

Furthermore, the use of a unified and validated classification system for papilla morphology is recommended to improve transparency, communication, and reproducibility in both clinical practice and training.

11.2. Study 2

Based on our results, patients presenting with HI should be identified early and managed as a high-risk population. In particular in UGIB, hemodynamically compromised patients require prompt assessment, early resuscitation, and close monitoring in an emergency or high-dependency setting.

The integration of a unified and clearly defined definition of HI or shock into routine clinical practice may improve early risk stratification and facilitate timely decision-making.

Given the markedly increased risks of in-hospital mortality, rebleeding, and the need for surgical intervention, early and aggressive stabilization, multidisciplinary involvement, and appropriate triage to higher levels of care are essential to improve clinical outcomes.

12. IMPLICATIONS FOR RESEARCH

12.1. Methodology and Study Design

12.1.1. Study 1

Large, well-characterized cohorts are needed to further validate the modified papilla morphology classification, including the assessment of PAD involvement. Beyond overall event rates, future studies should also evaluate the severity of PEP across different papilla types to better capture clinically relevant outcomes.

12.1.2. Study 2

High-quality RCTs are needed to define optimal early resuscitation strategies in hemodynamically unstable patients with acute GIB. In addition, future interventional studies should examine the interaction between resuscitation intensity and the timing of endoscopy to better delineate safe and effective early management strategies.

12.2. New Areas

12.2.1. Study 1

Future research should consider the development of morphology-based recommendation systems for advanced biliary cannulation techniques to support procedural planning and technique selection. Beyond procedural guidance, the role of papilla morphology as a component of integrated ERCP risk stratification frameworks deserves further investigation.

12.2.2. Study 2

Further prospective cohort studies should investigate modifiable factors contributing to the development of initial HI, including comorbidities, medication use, and delays in early care. Moreover, research focusing on prehospital and emergency department triage parameters may improve early identification of high-risk patients and enable more timely escalation of care.

13. IMPLICATIONS FOR POLICY MAKERS

13.1. Study 1

From a policy perspective, our findings underline the importance of structured education, standardization, and data-driven quality improvement in ERCP practice. Given the impact of papilla morphology on procedural difficulty and adverse events, dedicated training programs should be supported, with particular emphasis on hands-on simulation and cadaver-based courses that allow trainees to safely practice fundamental cannulation techniques before performing high-risk procedures in clinical settings.

Furthermore, structured supervision frameworks and competency-based progression in ERCP training may contribute to improved patient safety and more consistent procedural outcomes.

In parallel, the development and dissemination of standardized patient education materials addressing potential ERCP-related adverse events, including post-ERCP pancreatitis, should be encouraged to improve informed consent and patient awareness.

At a system level, the implementation of uniform endoscopic reporting standards, including mandatory documentation of papilla morphology using a validated classification system, may enhance transparency and comparability across centers. The establishment or further development of national endoscopy registries with standardized data collection could facilitate continuous quality monitoring, benchmarking, and research.

13.2. Study 2

At a health system level, our findings support the implementation of standardized, pathway-based emergency management for acute GIB with HI. Because HI at presentation — particularly in UGIB — identifies a subgroup with markedly increased odds of mortality, rebleeding, and the need for surgery, patients meeting HI criteria should be triaged as high priority and managed within dedicated resuscitation pathways. A unified, operational definition of HI and shock should be embedded into routine clinical practice and reporting to enable consistent risk stratification and timely escalation of care.

In addition, system-level protocols should prioritize early recognition, prompt resuscitation, and stabilization before proceeding to definitive endoscopic therapy. Finally, standardized monitoring and post-acute care pathways, combined with registry-based quality indicators (e.g., time to stabilization and outcomes among patients with HI), may facilitate benchmarking and continuous quality improvement across centers.

14. FUTURE PERSPECTIVES

Acute gastrointestinal conditions represent some of the most time-critical and complex scenarios in gastroenterology, where early decision-making and procedural performance have a direct impact on patient outcomes. As an interventional endoscopist in training, my long-term goal is to contribute to the optimization of acute gastrointestinal care, with particular emphasis on the early phase of patient assessment and intervention.

The findings of this thesis highlight two complementary pillars of high-quality acute care: precise risk stratification at presentation and technically informed endoscopic management. In patients undergoing ERCP, systematic assessment of major papilla morphology at the start of the procedure may support safer cannulation strategies, improve training pathways, and reduce procedure-related adverse events. In parallel, early recognition of HI in acute GIB is crucial for identifying high-risk patients who require prompt resuscitation, intensified monitoring, and appropriately timed endoscopic intervention.

Building on these results, I aim to support the integration of these principles into routine clinical practice through targeted education, improved standardization, and collaborative, data-driven approaches. This includes structured training focusing on anatomical recognition and risk-adapted technique selection, the use of unified definitions and standardized documentation in acute gastrointestinal emergencies, and active participation in prospective registries and multicenter collaborations. Ultimately, these efforts aim to enhance early clinical and endoscopic decision-making, thereby contributing to safer and more consistent acute gastrointestinal care, and supporting the development and implementation of evidence-based care pathways.

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16. BIBLIOGRAPHY

16.1. Publications related to the thesis

1. **Tari, Edina** ; Gagyi, Endre Botond ; Rancz, Anett ; Veres, Dániel Sándor ; Váncsa, Szilárd ; Hegyi, Péter Jenő ; Hagymási, Krisztina ; Hegyi, Péter ; Erőss, Bálint
Morphology of the papilla can predict procedural safety and efficacy of ERCP-a systematic review and meta-analysis.
SCIENTIFIC REPORTS (2024)
Publication: 34763940
Journal subject: Scopus - Multidisciplinary Rank: Q1
IF: 3.9

2. **Tari, Edina** ; Frim, Levente ; Stolcz, Tünde ; Teutsch, Brigitta ; Veres, Dániel Sándor ; Hegyi, Péter ; Erőss, Bálint
At admission hemodynamic instability is associated with increased mortality and rebleeding rate in acute gastrointestinal bleeding : a systematic review and meta-analysis
THERAPEUTIC ADVANCES IN GASTROENTEROLOGY (2023)
Publication: 34123722
Journal subject: Scopus - Gastroenterology Rank: Q1
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16.2. Publications not related to the thesis

3. **Tari, E.** ; Vörhendi, N. ; Kiss, S. ; Teutsch, B. ; Váradi, A. ; Sisák, K. ; Alizadeh, H. ; Hegyi, P. ; Erőss, B.
Anaemia Is Associated with an Increased Risk of Fractures, a Systematic Review, and Meta-Analysis
GERONTOLOGY (2023)
Publication: 32758286
Journal subject: Scopus - Geriatrics and Gerontology Rank: Q2
Journal subject: Scopus - Aging Rank: Q3
IF: 3.1

4. Boros, Eszter ; Pintér, József ; Molontay, Roland ; Prószéky, Kristóf Gergely ; Vörhendi, Nóra ; Simon, Orsolya Anna ; Teutsch, Brigitta ; Pálinkás, Dániel ; Frim, Levente ; **Tari, Edina** et al.
New machine-learning models outperform conventional risk assessment tools in Gastrointestinal bleeding
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Publication: 35785849
Journal subject: Scopus - Multidisciplinary Rank: Q1
IF: 3.9

5. Floria, Diana-Elena ; Fogarasi, Beatrix ; **Tari, Edina** ; Szabó, László ; Sándor Veres, Dániel ; Sára Bognár, Anna ; Sikó, Beáta ; Erőss, Bálint ; Teutsch, Brigitta ; Hegyi, Péter
Psychological interventions improve mental health in inflammatory digestive diseases : a systematic review and meta-analysis of randomized controlled trials
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Publication: 36411906
Journal subject: Scopus - Gastroenterology Rank: Q1
IF: 3.4

6. Gagyi, Endre Botond ; Obeidat, Mahmoud ; **Tari, Edina** ; Váncsa, Szilárd ; Veres, Daniel Sandor ; Banovcin, Peter ; Hegyi, Peter Jeno ; Hegyi, Peter ; Eross, Balint
Progression from acute to chronic pancreatitis in children : a systematic review and meta-analysis
CLINICAL AND EXPERIMENTAL PEDIATRICS (2025)
Publication: 36490540
Journal subject: Scopus - Pediatrics Rank: D1
Journal subject: Scopus - Pediatrics, Perinatology and Child Health Rank: Q1
IF: 3.6

7. Teutsch, B. ; Tóth, Z.A. ; Ferencz, O. ; Vörhendi, N. ; Simon, O.A. ; Boros, E. ; Pálinkás, D. ; Frim, L. ; **Tari, E**. ; Kalló, P. et al.

Hemoglobin decrease predicts untoward outcomes better than severity of anemia

SCIENTIFIC REPORTS (2024)

Publication: 35663428

Journal subject: Scopus - Multidisciplinary Rank: Q1

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8. Obeidat, Mahmoud ; Teutsch, Brigitta ; Rancz, Anett ; **Tari, Edina** ; Márta, Katalin ; Veres, Dániel Sándor ; Hosszúfalusi, Nóra ; Mihály, Emese ; Hegyi, Péter ; Erőss, Bálint

One in four patients with gastrointestinal bleeding develops shock or hemodynamic instability : A systematic review and meta-analysis

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