# Retrospective population-based study on epidemiology of acute mesenteric ischemia in Estonia

**Study Protocol (AMI version1.0)**

**01.04.2021**

**Principal Investigator**

Karri Kase, MD
Tartu University Hospital, Department of Surgery
Estonia, Tartu City, Puusepa 8
+3727318065
karri.kase@kliinikum.ee

**Sub Investigators**

Peep Talving, MD, PhD
The North Estonia Medical Centre, Clinical director, professor of surgery
Estonia, Tallinn City, J. Sütiste 19
+3726171525
peep.talving@ut.ee

Annika Reintam Blaser, MD, PhD
University of Tartu, Department of Anaesthesiology and Intensive Care and Luzerner Kantonsspital, Department of Intensive Care Medicine
Estonia, Tartu City, Puusepa 8
+3725142281
annika.reintam.blaser@ut.ee

Kadri Tamme , MD, PhD
Tartu University Hospital, Department of Anaesthesiology and Intensive Care
Estonia, Tartu City, Puusepa 8
+3727318414
kadri.tamme@kliinikum.ee

Marko Murruste, MD
Tartu University Hospital, Department of Surgery
Estonia, Tartu City, Puusepa 8
+3727318065
marko.murruste@kliinikum.ee

Olga Kiss, MD
Tartu University Hospital, Department of Anaesthesiology and Intensive Care
Estonia, Tartu City, Puusepa 8
+37253363610
olga.kiss@kliinikum.ee

Sergei Gordienko, MD

Tartu University Hospital, Department of Anaesthesiology and Intensive Care
Estonia, Tartu City, Puusepa 8
+37258503358
Sergei.gordienko@kliinikum.ee

Martin Kivilo
University of Tartu, Faculty of Medicine
+3725176217
martinkivilo@gmail.com

**Funding Sponsor**

Study is funded by Grant PRG 1255 (duration 2021-2025).

**Summary**

Title: Retrospective population-based study on epidemiology of acute mesenteric ischemia in Estonia

Protocol number: AMI version1.0

Study Design/Methodology: Retrospective population-based study

Study duration: April 2021 until December 2022

Study Center: primary study center: Tartu University Hospital, patients from all hospitals in Estonia included.

Objectives: to describe epidemiologic features in adult patients with acute mesenteric ischemia

Number of subjects: 500

Eligibility criteria: all at least 18-year-old patients with acute mesenteric ischemia during years 2016-2020.

Study interventions: none

## Background

This study is a retrospective population-based study on epidemiology of acute mesenteric ischemia in Estonia.

Acute mesenteric ischemia (AMI) is a potentially fatal vascular emergency with overall mortality of 60-80% (1). Acute mesenteric ischemia comprises a group of pathophysiologic processes that have a common end point – insufficient blood supply to the bowel leading to bowel ischemia and if blood supply is not restored fast, to transmural bowel necrosis (infarction):

1. Occlusive mesenteric ischemia:
   a. Arterial thrombosis
   b. Arterial embolism
   c. Venous thrombosis
2. Non-occlusive mesenteric ischemia (NOMI)

There are no previous studies about the incidence of acute mesenteric ischemia in Estonia.

Between 1970 and 1982 in Malmö (Sweden) autopsies were conducted on as many as 87% of the deceased in the population of approximately 250 000 inhabitants. They found that the annual incidence of AMI was 12 per 100 000 inhabitants. (2). There has not been comparable study to Malmö cohort.

Between 2009 and 2013 Kärkkäinen JM et al studied patients with acute abdomen and found that the incidence rate of AMI was 7,3/100 000/year. (3).

Considering that population is aging and AMI primarily affects elderly then potentially incidence of AMI should increase. However, abovementioned studies suggest that it may rather decrease. Reasons for that could be better control and treatment of comorbidities. For example such development has been shown for cardiovascular events. (4)(5).

There are no large studies about the risk factors of AMI, but the main etiologic factor is atherosclerosis. (6).

Beaulieu and colleagues found a total of 23744 hospital admissions for AMI registered in the Nationwide Inpatient Sample database from 2005 to 2009. Only 3% received an attempt of open or endovascular revascularization, while 17% were treated with bowel resection alone, and 80% received no intervention whatsoever. (7).

Meanwhile studies have shown that correct diagnosis in right time and subsequent adequate treatment could potentially save more than half of AMI patients. (8).

According to this acute mesenteric ischemia needs definitely greater interest and continuing studies to improve diagnostics and treatment.

**Study objectives**

Primary objective:

To identify the incidence of AMI in adult hospitalized patients in Estonia during 2016-2020.

Secondary objectives:

To describe the phenotype of AMI.

To describe treatment modalities and outcome of AMI.

Results obtained from this study will be used for designing a prospective multi-center study about AMI.

**Study design and methods**

Sample size

1. Previous studies (1-3) have found that incidence of AMI could be 6-12/100 000/year.
2. We do not have exact primary data about AMI in Estonia and that is why we could not calculate precise sample size. We assume that 500 patients with AMI is sufficient to describe also different subgroups (see above).
3. In view of prior we plan to analyze data from 5 years and will collect the most recent data (years 2016-2020).

Study data

To identify the patients of interest, we ask Estonian Health Insurance Fund to extract data for all cases where diagnostic and procedure codes covering acute mesenteric ischemia during years 2016-2020 have been documented.
Diagnostic codes (ICD-10) and procedure codes (NOMESCO) that cover acute mesenteric ischemia:

1. ICD-10: I74.0, I74.1, I74.8, I74.9, I81, K55.0, K55.1, K55.8, K55.9
2. NOMESCO: PCE30, PCF30, PCG30, PCH30, PCJ30, PCK30, PCN30, PCP30, PCQ30, PCR30, PCT30

We ask for the following information for each patient:

1. Number of case
2. Personal identification code
3. When and where (name of the hospital) this patient was hospitalized with respective diagnostic code

From these patients we will identify those who truly have AMI, based on the following criteria:

- Occlusive acute mesenteric ischemia:

a. appropriate clinical presentation of life-threatening acute intestinal ischemia with
b. thrombosis or embolism of the mesenteric arteries or thrombosis of the mesenteric veins and
c. either presence of pathological intestinal findings on a computer tomography (CT) scan (bowel wall thickening, abnormal bowel wall enhancement, or luminal dilatation) or bowel necrosis identified at laparoscopy/laparotomy/autopsy.

- Nonocclusive mesenteric ischemia (NOMI):
  a. acute intestinal ischemia based on clinical presentation pattern and
  b. pathological intestinal findings on a CT scan or bowel necrosis on laparoscopy/laparotomy or autopsy
  c. without significant (<70 %) obstruction of the superior or inferior mesenteric artery.

The primary data screening will be performed by the principal investigator using Estonian Health Information System.

For patients who likely had AMI, data collection from medical case charts will be initiated.

Data collection in different hospitals will be organized by the principal investigator.

Also, we ask from Estonian Health Insurance Fund the total number of adult patients admitted to different Estonian hospitals for years 2016-2020 to calculate the incidence of AMI in adult hospitalized patients.

From Estonian Causes of Death Registry we ask data about all cases of death of the patients with acute mesenteric ischemia in the final database and their death certificate diagnoses to identify mortality outcome.

Database

The exact data that will be collected are shown in Annex 1.

All data will be entered in a Microsoft Excel database. The data will be pseudonymised - each patient will be assigned a unique study-ID. The key, to identify patients will be stored separately from the database on a secure server of Tartu University Hospital in a password protected file and can be accessed only by the principal investigator. Database will be stored separately from the key on a server of Tartu University Hospital in a password protected file and can be accessed by study investigators.

Statistical analysis

The study population will be described using common statistics (minimum, maximum, mean with standard deviation or median with interquartile range, standard error). The software package Statistica version 13.3 (TIBCO Software, California, USA) will be used for statistical calculations.

## Ethical Considerations

Our study is retrospective and descriptive, there is no intervention and researchers do not intercede.

Data protection

In the study it is necessary to use personalized medical data, because queries from different registries are made using the personal identification code. The study aims cannot be fulfilled using anonymous data.

Data will be processed without the data subject's consent. Asking for informed consent is not possible as AMI has high mortality and most of these patients are not available for asking informed consent. Omitting these patients would seriously decrease the quality of the study.

Measures to safeguard the fundamental rights and the interests of the data subject:

- From Estonian Health Insurance Fund and Estonian Causes of Death Registry all data will be sent in encrypted form and will be decrypted by the principal investigator.
- Only pseudonymised data will be entered in the database. Each patient will be assigned a unique study-ID. The key, to identify patients will be stored separately from the database on a secure server of Tartu University Hospital in a password protected file and can be accessed only by the principal investigator. Database will be stored separately from the key on a server of Tartu University Hospital in a password protected file and can be accessed only by study investigators.
- Medical case files will not be sent via Internet or post. The principal investigator will go to the hospitals and enter the data to the database there.
- Only pseudonymized data will be used for data analysis and publication of results.
- The key to identify patients will be destroyed 3 years after the end of the study (31.12.2025)
- After the key is destroyed the database becomes anonymous. The anonymous database will be kept for 15 years.

Data controller: University of Tartu.

The collected data are going to be used only for publishing scientific articles about acute mesenteric ischemia. No information that allows identification of the study subjects will be published.

Data will not be used for financial purposes.

The Study has been approved by Research Ethics Committee of the University of Tartu (337/T-20). Approval of Estonian Committee of Bioethics and Human Research will be obtained.

## References


1. Oldenburg WA et al. Acute mesenteric ischemia: A Clinical Review. Arch Intern Med. 2004;164:1054-1062
2. Acosta S. Epidemiology of mesenteric vascular disease: clinical implications. Semin Vasc Surg 2010;23(1):4-8
3. Kärkkäinen JM et al. Acute mesenteric ischemia is a more common cause than expected of acute abdomen in the elderly. J Gastrointest Surg 2015;19(8):1407-14
4. Salomaa V et al. Aging of the population may not lead to an increase in the numbers of acute coronary events: a community surveillance study and modelled forecast of the future. Heart 2013;99(13):954-9
5. Borodulin K et al. Forty-year trends in cardiovascular risk factors in Finland. Eur J Public Health 2015;25(3):539-46
6. Lehtimäki TT et al. Detecting acute mesenteric ischemia in CT of the acute abdomen is dependent on clinical suspicion: review of 95 consecutive patients. Eur J Radiol 2015;84(12):2444-53
7. Beaulieu RJ et al. Comparison of open and endovascular treatment of acute mesenteric ishemia. J Vasc Surg 2014;59(1):159-64
8. Kärkkäinen JM et al. Endovascular therapy as a primary revascularization modality in acute mesenteric ischemia. Cardiovasc Interv Radiol 2015;38(5):1119-29

**Annex 1**

Data that will be collected

1. General
    a. Gender (M/F)
    b. Age (y)
    c. Hospital
2. Health condition
    a. Disability (no need of assitance/needs/No information(NI))
    b. Consciousness (Adequate/Disturbed/No contact/NI)
    c. Weight (kg/NI)
    d. Height (cm/NI)
    e. BMI ($kg/m^2$)
    f. Smoking (yes/no/NI)
3. Diagnoses
    a. Atrial Fibrillation (yes/no/NI)
    b. Atherosclerosis (yes/no/NI)
    c. Hypertonic disease (yes/no/NI)
    d. Hypercholesterolemia (yes/no/NI)
    e. Previous myocardial infarction (yes/no/NI)
    f. Previous thromboembolic events (yes/no/NI)
    g. Artificial heart valve (yes/no/NI)
4. Diagnoses II
    a. Important main or accompanying pathology
5. Mediactions
    a. Anticoagulant drugs (yes/no/NI)
    b. Antiplatelet drugs (yes/no/NI)
    c. Statins (yes/no/NI)
6. Emergency Department
    a. Arrival to hospital (by self, ambulance)
    b. Occured during hospital treatment (then yes here, and previous is left empty)
    c. Arrival to hospital since the beginning of symptoms (hours (h)/unclear)
    d. Time from admition to hospital since CT-scan (h)
    e. Time from beginning of symptoms to diagnoosis (h)
    f. Time from arrival to hospital since diagnoosis (h)
7. Laboratory tests
    a. Lactate (mmol/l/NI)
    b. WBC (x 10E9/L/NI)
    c. Creatinine (mcmol/l/NI
    d. eGFR (mL/min/1,73m27/NI)
    e. BE (mmol/l/NI)
    f. ASAT (U/L/NI)
    g. Amylase (U/L/NI)
    h. D-dimers (mg/L/NI)
    i. Troponin T (ng/L/NI)

8. Radiography
    a. What was the first radiographic study (x-ray, US, CT/NI)
    b. Was there a CT-scan made (yes/no)
    c. Phase of enhancement in CT-scan (no contrast media, portal venous, arterial, delayed phase)
    d. Radiologist diagnosed AMI (yes/no)
    e. Time between CT-scan and the response by radioloogist (min)
9. Type of AMI
    a. Arterial embolism (a. mes. sup. – aortic ostium, until separation of a. colica media, peripheral)
    b. arterial thrombosis (a. mes. sup. – aortic ostium, until separation of a. colica media, peripheral)
    c. arterial non specified (a. mes. sup. – aortic ostium, until separation of a. colica media, peripheral)
    d. Venous
    e. NOMI
    f. Other location (truncus coealiacus or a. mes. inf.)
    g. Unclear
10. Treatment
    a. Time from beginning of symptoms to treatment (h)
    b. Time from diagnosis to treatment (h)
    c. Surcigal tactics (diagnostic laparoscopy, diagnostic laparotomy, therapeutic laparotomy, second-look tactics)
    d. Vascular tactics (embolectomy, thrombectomy, endarterectomy, aortomesenteric shunt)
    e. Gastrointestinal tactics (no need, resection with primary anastomosis, resection with stoma formation, resection without anastomosis and second look)
    f. Intestinal resection (cm/NI)
    g. Resection of colon (no need, right hemicolectomy, subtotal colectomy)
    h. Endovascular treatment (aspiration of thrombus/embolism, ballondilatation, stent placement, thrombolysis, combined)
    i. Conservative treatement
    j. End-of-life care
11. Hospital treatment
    a. Duration
    b. End (discharged, death)
    c. 30 day survival (alive/dead)
    d. 90 day survival (alive/dead)
    e. 180 day survival (alive/dead)
    f. 360 day survival (alive/dead)