Demographics, diagnosis, management, and outcomes of non-occlusive mesenteric ischemia: a substudy of a prospective multicenter observational study (AMESI)

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Summary

Title: Demographics, diagnosis, management, and outcomes of non-occlusive mesenteric ischemia: a preplanned analysis of AMESI study.

Protocol number: 1

Study Design/Methodology: Prospective multicenter observational study

Study duration (recruitment period): 06 June 2022 – 05 April 2023

Objectives: The primary objective of this study is to describe the demographic profile, clinical presentation, and laboratory findings of patients with non-occlusive mesenteric ischemia (NOMI). The secondary objective is to find independent risk factors for NOMI and to outline the diagnostics, management strategies, and outcomes of these patients, including in-hospital results and outcomes at 90 days and one year.

Number of subjects: Patients with NOMI (n= 55), arterial occlusive AMI (n=231), venous occlusive AMI (n=73), unclear mechanism of AMI (n=48) and patients with suspected but not confirmed AMI (n=159), in total 566 patients. 2

Eligibility criteria: all at least 18-year-old patients with acute mesenteric ischemia or patients suspected of acute mesenteric ischemia that was not confirmed.

Background

The current study is a preplanned substudy of a prospective observational multicenter study: Incidence, diagnosis, management and outcome of acute mesenteric ischemia: a prospective, multicenter observational study (AMESI Study) [1].

Non-occlusive mesenteric ischemia (NOMI) is a subtype of acute mesenteric ischemia (AMI) where insufficient mesenteric perfusion occurs without occlusion of large mesenteric arteries [2]. AMI is a rare condition. According to a systematic review and meta-analysis published in 2022, the mean incidence was 6.2 cases per 100 000 person-years [3]. Out of all AMI cases, NOMI accounts for 7 - 30% [1–5]. NOMI was identified in only 13 of the 32 sites in the AMESI study, with proportions varying from 0% to 50%. Furthermore, 11.5% out of all confirmed AMI patients had an unclear mechanism, which might represent NOMI. One reason for variability in NOMI identification stems from both a lack of awareness and the inherent difficulty in diagnosing the disease [6]. Due to its rarity, there is a lack of descriptive information available in the literature and consistent demographic, clinical, and laboratory patterns are not recognized.

NOMI is challenging to diagnose due to its non-specific symptoms and lack of large vessel occlusion. Clinical examination and routine laboratory tests are of only little value in reaching an early and reliable diagnosis of NOMI [5]. Computed tomography (CT) angiography is considered a gold standard for detecting arterial occlusive mesenteric ischemia [7]. Unfortunately, the diagnostic accuracy of CT angiography in detecting NOMI is relatively low. In a study by Bourcier et al., 25% of patients diagnosed with NOMI showed no signs of mesenteric ischemia on the CT scan [8,9]. One of the reasons for this is the absence of specific diagnostic criteria [5]. The diagnostic ambiguity means the true incidence of NOMI could be higher than currently reported. By outlining the diagnostic patterns observed in patients with NOMI, we may uncover clinical, imaging, or laboratory findings that improve the recognition of this condition.

There are currently no specific management guidelines for NOMI. Consequently, the treatment of this condition is based on limited evidence and varies across different institutions and clinicians [5]. Describing the management of NOMI patients might contribute to the development of more systematic and evidence-based management strategies.

The aim of this substudy is to describe the demographic profile, clinical presentation, and laboratory findings of patients with non-occlusive mesenteric ischemia in comparison to

other subtypes of acute mesenteric ischemia and patients with suspected but not confirmed acute mesenteric ischemia. Furthermore, we aim to identify independent risk factors of NOMI and to describe the diagnostics, management strategies, and outcomes of these patients.

Study questions

1. What are the differences in demography, chronic and acute health conditions, clinical symptoms, laboratory values, time factors, diagnostics, management, and outcomes between patients with NOMI and those with other subtypes (arterial occlusive, venous) of AMI?

2. What are the differences in demography, chronic and acute health conditions, clinical symptoms, laboratory values, time factors, and outcomes between patients with NOMI and AMI with an unclear mechanism?

3. Which demographic, chronic and acute health conditions, clinical symptoms, and laboratory values are independently associated with NOMI compared to patients with suspected but not confirmed AMI?

   3.1. Subgroup analysis: NOMI vs suspected but not confirmed AMI in the ICU patients.

4. Which diagnostic methods are used to identify NOMI, and which for AMI with an unclear mechanism?

5. Which management strategies are used for NOMI, and which for AMI with an unclear mechanism?

6. What are the differences in demography, chronic and acute health conditions, clinical symptoms, laboratory values, and outcomes between NOMI patients managed surgically and conservatively?

   6.1. Which factors predict the effectiveness of conservative management (survival without abdominal surgery)?

7. What are the outcomes in patients with NOMI?

8. What are the risk factors of mortality in patients with NOMI?

   7.1. What are the risk factors of mortality in patients with NOMI who received treatment without withdrawal of care?

Study design and methods

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Inclusion criteria for the substudy

- Patients with arterial occlusive AMI
- Patients with non-occlusive mesenteric ischemia
- Patients with venous occlusive AMI
- Patients with unclear mechanism of AMI
- Patients with suspected but not confirmed AMI

Exclusion criteria for the substudy

- Patients with other specific form of AMI (e.g dissection)
- Confirmed strangulating bowel obstruction

Study groups

- Patients with non-occlusive mesenteric ischemia.
- Patients with arterial occlusive AMI
- Patients with venous occlusive AMI
- Patients with unclear mechanism of AMI
- Patients with suspected but not confirmed AMI
- Patients with suspected but not confirmed acute mesenteric ischemia
    - Patients with suspected but not confirmed acute mesenteric ischemia treated in the ICU

The comparative groups are presented in Annex 1, and the variables included in the study are presented in Annex 2.

Study question analysis

1. What are the differences in demography, chronic and acute health conditions, clinical symptoms, laboratory values, time factors, diagnostics, management, and outcomes between patients with NOMI and those with other subtypes (arterial occlusive, venous) of AMI?

Patients with NOMI, arterial occlusive, venous occlusive AMI will be analysed. These patients will be divided into groups – NOMI vs other subtypes (arterial occlusive, venous occlusive) of AMI. The groups (NOMI vs arterial occlusive; NOMI vs venous occlusive) will be compared with each other. Normality will be assessed with the Kolmogrov-Smirnov test.

If the variables follow a normal distribution, means and standard deviations will be used to present the data. However, if the data is not normally distributed, medians and interquartile ranges will be used instead. Categorical data will be represented with n (%). To compare the two groups, a t-test, a Chi-square test, or Mann-Whitney U test will be used. Statistical significance will be defined as $p < 0.05$.

Parameters used for analysis are depicted in Annex 2 subsections, A. NOMI vs arterial occlusive AMI and B. NOMI vs venous occlusive AMI. The variables included are the following: demographic description, chronic health conditions, acute health conditions, symptoms supporting AMI diagnosis, laboratory values, time factors, diagnostics, management, and outcomes.

2. What are the differences in demography, chronic and acute health conditions, clinical symptoms, laboratory values, time factors, and outcomes between patients with NOMI and AMI with an unclear mechanism?

Patients with NOMI and unclear mechanism of AMI will be analysed. These patients will be divided into groups – NOMI vs unclear mechanism of AMI. The two groups will be compared with each other. Normality will be assessed with the Kolmogrov-Smirnov test. If the variables follow a normal distribution, means and standard deviations will be used to present the data. However, if the data is not normally distributed, medians and interquartile ranges will be used instead. Categorical data will be represented with n (%). To compare the two groups, a t-test, a Chi-square test, or Mann-Whitney U test will be used. Statistical significance will be defined as $p < 0.05$.

Parameters used for analysis are depicted in Annex 2 subsection C. NOMI vs unclear mechanism of AMI. The following categories are included: demographic description, chronic health conditions, acute health conditions, symptoms supporting AMI diagnosis, laboratory values, time factors, and outcomes.

3. Which demographic, chronic and acute health conditions, clinical symptoms, and laboratory values are independently associated with NOMI compared to patients with suspected but not confirmed AMI?

All NOMI patients and those with suspected but not confirmed AMI will be included in the analysis. These patients will be divided into groups – NOMI vs suspected but not confirmed AMI. The two groups will be compared with each other. A separate subgroup comparison will

be conducted between patients with NOMI and ICU patients with suspected but not confirmed AMI. Normality will be assessed with the Kolmogrov-Smirnov test. If the variables follow a normal distribution, means and standard deviations will be used to present the data. However, if the data is not normally distributed, medians and interquartile ranges will be used instead. Categorical data will be represented with n (%). To compare the two groups, a t-test, a Chi-square test, or Mann-Whitney U test will be used. Statistical significance will be defined as $p < 0.05$.

To find demographic, acute, and chronic health variables, symptoms, and laboratory tests that are independently associated with the occurrence of NOMI, univariable regression models for the occurrence of NOMI will be fitted. All risk factors with p-value < 0.1 will be entered into multivariate regression model to determine the independent associations. Variables showing p-values < 0.05 in the multivariable model will be considered independent risk factors for the occurrence of NOMI.

Parameters used for analysis are depicted in Annex 2 subsection D. NOMI vs suspected but not confirmed AMI and E. NOMI vs suspected but not confirmed AMI in the ICU. The following categories are included: demographic description, chronic health conditions, acute health conditions, symptoms supporting AMI diagnosis, and laboratory values.

4. Which diagnostic methods are used to identify NOMI, and which for AMI with an unclear mechanism?

Patients with NOMI and unclear mechanism of AMI will be analysed. These patients will be divided into groups – NOMI vs unclear mechanism of AMI. The two groups will be compared with each other. Data will be presented as numbers and proportions. To compare the two groups, the Chi-square test or Fisher's exact test will be used, as appropriate. Statistical significance will be defined as $p < 0.05$.

Parameters used for analysis are depicted in Annex 2 subsection C. NOMI vs unclear mechanism of AMI. Only the diagnostics category will be included in the analysis.

5. Which management strategies are used for NOMI, and which for AMI with an unclear mechanism?

Patients with NOMI and unclear mechanism of AMI will be analysed. These patients will be divided into groups – NOMI vs unclear mechanism of AMI. The two groups will be compared with each other. Data will be presented as numbers and proportions. To compare the two groups, the Chi-square test or Fisher's exact test will be used, as appropriate. Statistical significance will be defined as $p < 0.05$.

Parameters used for analysis are depicted in Annex 2 subsection C. NOMI vs unclear mechanism of AMI. Only the management category will be included in the analysis.

6. What are the differences in demography, chronic and acute health conditions, clinical symptoms, laboratory values, and outcomes between NOMI patients managed surgically vs conservatively?

All patients with NOMI will be included in the analysis. NOMI patients will be separated into two groups based on management – surgical vs conservative. Data will be presented as numbers and proportions. A separate subgroup comparison will be made between patients with effective conservative management (defined as hospital survival without surgical intervention) and those who died during conservative management or required surgical intervention after initial conservative management. For continuous variables normality will be assessed with the Kolmogrov-Smirnov test. If the variables follow a normal distribution, means and standard deviations will be used to present the data. However, if the data is not normally distributed, medians and interquartile ranges will be used instead. To compare the two groups, a t-test, Chi-square test, or Mann-Whitney U test will be used. Statistical significance will be defined as $p < 0.05$.

Parameters used for analysis are depicted in Annex 2 subsections, F. Conservatively managed NOMI vs surgically managed NOMI and G. Effective conservative NOMI management vs ineffective conservative and surgically managed. The following categories are included: demographic description, chronic health conditions, acute health conditions, symptoms supporting NOMI diagnosis, laboratory values, and outcomes.

7. What are the outcomes in patients with NOMI?

Only patients with NOMI will be analysed. Data will be presented as numbers and proportions. If the variables follow a normal distribution, means and standard deviations will be used to present the data. However, if the data is not normally distributed, medians and interquartile ranges will be used instead.

Parameters used for analysis are depicted in Annex 2 subsection H. NOMI outcomes. Only the outcomes category will be included in the analysis.

8. What are the risk factors of mortality in patients with NOMI?

Only patients with NOMI will be analysed. To find the potential risk factors we will enter all potential risk factors for mortality among NOMI patients into univariable model. A separate subgroup analysis will be performed among NOMI patients who received treatment without withdrawal of care. All variables showing p-values <0.1 will be entered into multivariable regression model to determine the independent associations. Variables showing p-value < 0.05 will be considered independent risk factors for mortality among NOMI patients.

Parameters used for analysis are depicted in Annex 2 subsections, I. Surviving NOMI vs deceased NOMI and J. Surviving NOMI vs deceased NOMI without withdrawal of care. NOMI. The following categories are included: demographic description, chronic health conditions, acute health conditions, symptoms supporting NOMI diagnosis, laboratory values, time factors, management, and ICU management.

Ethical considerations

Since this is an analysis of a pseudonymized database from an Ethics Committee approved study (EC of the University of Tartu, 357/T-8 and 364M-7), no separate ethical approval is required.

References:

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