

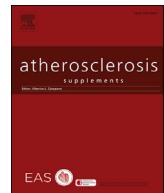


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Improving lipid management in patients with acute coronary syndrome: The ACS Lipid EuroPath tool

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ABSTRACT

Keywords:

Acute coronary syndrome
Dyslipidemia
Lipids
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Self-assessment

Post-acute coronary syndrome (ACS) patients are at very high risk for recurrent events and mortality, despite the availability of effective pharmacological approaches. In 2018, the ACS EuroPath Survey, performed in collaboration with 555 European cardiologists, identified a sub-optimal LDL-C management in post-ACS patients.

Based on these premises, the ACS EuroPath II project led to the development of a self-assessment tool to improve lipid management in these very high risk patients, taking into consideration the new 2019 ESC/EAS guidelines. This tool is built in 3 sections. The first is a questionnaire to assess the lipid management practice from the acute phase up to 12 months of follow-up. The main topics covered in this section relate to 1) acute phase (lipid management of ACS patients during hospitalization; 2) discharge (lipid management at discharge, with focus on follow-up plan); 3) follow-up (lipid management at the time of first and subsequent follow-ups); 4) referral pathway for definitive lipid management care of post-ACS patients; 5) evaluation of the achieved goal at 6 months to 1 year and key implications. The second section is a brief report to position the results against other European Union clinical practice and European guidelines. The last section allows the physician to evaluate and consider the implementation of one or more strategies, successfully developed in leading European centers, in order to optimize their own clinical practice.

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1. Introduction

Acute coronary syndrome (ACS) patients remain at very high risk for recurrent events and mortality, despite availability of effective pharmacological approaches [1,2]. In 2018, the ACS EuroPath I survey, performed in collaboration with 555 European cardiologists and 2775 patient records, demonstrated a sub-optimal LDL-C management after ACS [3]. However, multiple initiatives

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Acute phase: Lipid profile management of ACS patients during hospitalisation

Practices regarding lipid testing in the acute phase

1. When during hospitalisation is the LDL-C level assessed? _____

2. For what percentage of ACS patients is the baseline LDL-C assessed during hospitalisation? _____

3. Which other analyses are performed during hospitalisation? (multiple choice possible)

Non HDL-C Triglyceride (TG)
 ApoB High-sensitivity C-reactive protein (hs-CRP)
 Lp(a) HbA1c

Glycaemia
Other. If other, please describe: _____

Focus on statin-naïve patients, practices regarding lipid lowering therapy in the acute phase

4. When during hospitalisation is the lipid-lowering treatment initiated for statin naïve patients? _____

5. What percentage of statin naïve patients at admission are discharged under high intensity statin treatment? _____

6. Is the initiation of ezetimibe on top of statin considered for some naïve statin patients during hospitalisation? _____

Focus on patients already on statin before the event, practices regarding lipid lowering therapy in the acute phase

7. For ACS patients already on statin, in what percentage would lipid-lowering therapy intensification be considered before discharge? _____

8. Which lipid lowering treatment intensification is considered during hospitalisation? (multiple choice possible)

Increase the dose of statin Initiate ezetimibe on top of the same dose of statin
 Intensify to the max tolerated dose of statin Initiate ezetimibe on top of the max tolerated dose of statin
 Other.

If other, please describe: _____

9. When during hospitalisation is the lipid lowering treatment adjusted for ACS patients already under statin? _____

Practices regarding FH screening in the acute phase

10. Is an FH screening done for ACS patients during hospitalisation? _____

11. Which clinical criteria are considered for FH screening during hospitalisation? (multiple choice possible)

Age at first CV event
 Lipids level
 Family History of CV disease
 Dutch score
 Simon Broome criteria
 Other.

If other, please describe: _____

Fig. 1. Lipid profile management of ACS patients during the acute phase (hospitalization).

from several European countries have shown that the implementation of robust algorithms/protocols for LDL-C management can result in a more effective translation of guideline recommendations into clinical practice and significantly increase the achievement of recommended LDL-C goals to reduce CV risk [4]. Based on these premises, the ACS EuroPath project led to the development of a self-assessment tool for physicians aimed at identifying potential areas of improvement in the management of these very high risk patients, taking into consideration the recommendations provided by the new 2019 ESC/EAS guidelines [5]. This self-assessment tool has been developed in collaboration with a team of 8 European cardiologists and lipidologists and is presented in this article.

2. Objectives of the self-assessment tool

The objectives of the self-assessment tool are to: 1) provide a snapshot of clinical practice at a given time (it does not require identifiable patient related data). It is based on simple questions to assess personal practice regarding post ACS lipid management. The tool is quick to use and data are only for personal use of the physician, 2) position the results with regard to current European clinical practice as highlighted by the 2018 ACS EuroPath I survey [3], and 3) help identify strengths and areas of optimization by comparing to current European guidelines and European local clinical practice.

3. Key topics covered by the self-assessment tool

The key topics covered in the self-assessment tool relate to the management of lipids in ACS patients from the hospitalization phase and during follow-up and has been organized in 3 sections: a

questionnaire, a report, and potential targets for optimization.

4. Questionnaire

The questionnaire allows the physician to insert patient information from acute admission to the follow-up phase and comprises four distinct sections: 1) acute phase (lipid management of ACS patients during hospitalization); 2) discharge (lipid management at discharge, with focus on follow-up plan); 3) follow-up (lipid management at the time of first and subsequent follow-ups); 4) referral pathway for lipid management of post-ACS patients; 5) evaluation of the achieved goal at 6 months to 1 year and key implications.

The acute phase section includes practices regarding lipid testing, lipid lowering therapy (with distinction between statin-naïve patients and patients already on statin at admission), and practices regarding the screening for heterozygous familial hypercholesterolemia (FH). Physicians must indicate when the LDL-C level is assessed, for what percentage of ACS patient LDL-C level is assessed at admission, and additional parameters evaluated (including total cholesterol, non-HDL-C, Lp(a), and glycaemia among others) during the acute phase (Fig. 1). Information regarding lipid-lowering therapy at admission is collected. For statin naïve patients, physicians must indicate when the lipid-lowering treatment is started after admission, the percentage of patients receiving high intensity statin post-event, and whether ezetimibe on top of statin is considered in specific subgroup of patients. For patients already on statin before the event, physicians should indicate the percentage of patients who had a lipid-lowering therapy intensification, the type of treatment intensification (dose increase, dose doubling, adding ezetimibe on top of maximally tolerated dose of statin, initiate PCSK9i, etc.), and when

Discharge: Lipid profile management of ACS patients at discharge

Focus on follow-up plan

12. Is a follow-up pathway standardised after an ACS event?

13. What is the percentage of ACS patients that have a first follow-up visit planned at discharge?

14. What percentage of ACS patients has a rehabilitation program planned at discharge?

Focus on LDL-C goal at discharge

15. Which LDL-C goal is usually targeted in clinical practice at the discharge of ACS patient? Please describe (with the unit):

16. Is there a specific LDL-C goal for ACS patients with a second vascular event within 2 years?
If yes, please describe the goal (with the unit):

Focus on discharge letter for HCPs involved in the follow-up

17. For what percentage of ACS patients is a discharge letter written with lipid profile guidance?

18. What is included in the discharge letter in regard to the lipid management? (multiple choice possible)

- Specific LDL-C goal
- Time for next LDL-C measurement
- Lipid treatment guidance if LDL-C goal is not reached
- Timing of follow-up visits
- Guidance on how to manage muscular symptoms during statin treatment
- Clinical criteria to refer back the patient in regard to lipid management
- Other.

If other, please describe:

Focus on guidance / material delivered to the patients

19. What is the percentage of ACS patients receiving material at discharge including lipid management guidance?

20. What is provided to the patient in the discharge material? (multiple choice possible)

- LDL-C goal
- Timeline for a follow-up visit for lipid management
- Lifestyle intervention (e.g. sport, diet)
- Follow-up plan
- Other.

If other, please describe:

Fig. 2. Lipid profile management of ACS patients at discharge.

the treatment is adjusted with regard to admission time (Fig. 1). A special section in the questionnaire is dedicated to the detection of patients with FH. Based on recommendations by ESC/EAS guidelines and the data provided by surveys in ACS patients (refs), physicians are asked to provide information on whether a screening protocol is applied in patients hospitalized for an ACS, and the clinical criteria considered for the screening (in particular age, family history of CVD, elevated lipid levels, and the clinical score used) (Fig. 1). This represents a significant point since, although several surveys have reported an increased incidence of FH among

ACS patients compared with the general population, the EuroPath I survey showed that only 18% of patients hospitalized for an ACS were screened for FH during the acute phase (Landmesser et al.) [3].

The discharge section focuses on four specific points: 1) follow-up plan, 2) LDL-C goal at discharge, 3) discharge letter addressed to the general practitioner (GP) involved in this phase, and 4) information provided to patients (Fig. 2). ESC/EAS guidelines recommend that ACS patients participate in a structured cardiac rehabilitation program, in order to improve adequate control of cardiovascular risk factors including lipid levels and improve

Follow-up phase: Lipid profile management of ACS patients after discharge

Lipid management practice at the time of the first follow-up

21. For what percentage of ACS patients is a LDL-C measurement performed for the first follow-up visit?

22. What percentage of ACS patients with unmet LDL-C goal has their lipid-lowering therapy changed at the first follow-up?

23. When after discharge does the first lipid lowering therapy intensification occur?

24. Which clinical criteria are considered for lipid-lowering therapy intensification during the follow-up? (multiple choice possible)

- Lipids level
- Previous therapy
- CV risk profile
- Tolerance
- Other.

If other, please describe:

25. Which lipid lowering treatment intensification is considered during the follow-up? (multiple choice possible)

- Increase the dose of statin
- Intensify to the max tolerated dose of statin
- Other.
- Initiate ezetimibe on top of the same dose of statin
- Initiate ezetimibe on top of max tolerated dose of statin
- Initiate PCSK9i on top of max tolerated dose of statin + ezetimibe

If other, please describe:

Lipid management practice at the time of subsequent follow-ups

26. For what percentage of ACS patients is a LDL-C measurement performed during the subsequent follow-up visits?

27. Is the lipid lowering therapy intensification reconsidered if the LDL-C goal is not reached after the first follow-up visit?

28. If yes, when after the first follow-up does the intensification occur?

Fig. 3. Lipid profile management of ACS patients after discharge (follow-up phase).

Referral pathway for definitive lipid management care of ACS patients**Referral pathway for definitive lipid management care of ACS patients****Practices regarding patients referral****29. Are there patient referral patterns for optimal lipid care?**

Practices regarding the referral for ACS patients with suspicion of FH**30. Is a referral pattern established for ACS patients with suspicion of FH?**

31. Specify which criteria (multiple choice possible)

- Age
- Lipids level on or without previous therapy
- Family History of CV disease
- Other.

If other, please describe:

32. How well are the referral pattern for ACS patients with suspicion of FH known by the stakeholders?

Practices regarding the referral for statin intolerant ACS patients**33. Is a referral pattern established for statin intolerant ACS patients?**

34. Specify which criteria (multiple choice possible)

- Biological testing
- Patients complains
- Other.

If other, please describe:

35. How well are the referral patterns for statin intolerant ACS patients known by the stakeholders?

Practices regarding the referral for ACS patients eligible to PCSK9 inhibitors initiation (under maximum lipid lowering therapy)**36. Is a referral pattern established for ACS patients eligible to PCSK9 Inhibitors initiation (under maximum lipid lowering therapy)?**

37. Specify which criteria (multiple choice possible)

- Lipids level
- Previous therapy
- CV risk profile
- Other.

If other, please describe:

38. How well are the referral patterns for ACS patients eligible to PCSK9 inhibitors known by the stakeholders?

Practices regarding the referral for other high risk ACS patients**39. For which other high risk ACS patients is there a referral pattern established? (multiple choice possible)**

- | | | |
|---|---|--|
| <input type="checkbox"/> Patients with polyvascular disease | <input type="checkbox"/> Patients with recurrent CV events | <input type="checkbox"/> Patients with stroke antecedent |
| <input type="checkbox"/> Patients with LDL-C > 100 mg/dL (2.6 mmol/L) | <input type="checkbox"/> Patients with kidney disease | <input type="checkbox"/> Other. If Other, please describe: |
| <input type="checkbox"/> Patients with diabetes | <input type="checkbox"/> Patients with low glomerular filtration rate | |

40. How well are the referral patterns established for other high risk patients known by the stakeholders?**Fig. 4.** Referral pathway for definitive lipid management of ACS patients.

overall survival following the acute event [6]. Of note, in the EuroPath I survey, only half of the patients had a rehabilitation/secondary prevention program planned during follow-up [3]. In this section, physicians are required to insert information regarding the follow-up planning, including participation in a rehabilitation program, and the indication of the LDL-C goal. Furthermore, details on the indications included in the discharge letter must be stated (including the LDL-C goal, time to next LDL-C evaluation, the pharmacological approach to be adopted in case LDL-C goal is not

reached, the timing for future follow-up visits) (Fig. 2). Finally, details on the information provided to the patient at discharge are also required, including indications on LDL-C goal, follow-up visit plan (including lipid profile monitoring), and lifestyle interventions (such as sport and diet) (Fig. 2).

The follow-up section includes information on lipid management practice at the time of the first follow-up visit and subsequent follow-ups (Fig. 3). This section focuses on the intensification of lipid-lowering therapy in those patients who did not achieve their

Overall outcomes**Overall outcomes at 6 months to 1 year & key implications****41. What percentage of ACS patients are reaching LDL-C < 70mg/dL (1.8 mmol/L) at the second follow-up visit with the first year after an ACS event?**

42. In light of the 2019 ESC guidelines, what percentage of ACS patients are reaching the new LDL-C goal of 55mg/dL (1.4 mmol/L) at 6 months to 1 year after ACS event?

43. Which parts of your local pathway would need to be refined and / or optimised? (multiple choice possible)

- Acute phase
- Discharge
- Follow-up
- Referral

Fig. 5. Outcomes at 6 months to 1 year.

LDL-C goal, and requires information on the clinical criteria considered for therapy intensification (such as lipid levels, individual CV risk profile, therapy tolerance) as well as the type of treatment intensification adopted (increase of statin dose, adding ezetimibe to the same statin dose or on top of the maximally tolerated dose, initiating a PCSK9 inhibitor). Furthermore, the timing of intensification of the therapy is required (Fig. 3).

The fourth section is focused on the referral pathway for lipid management of post-ACS patients, with special attention for patients suspected of FH, statin-intolerant patients, patients eligible for a PCSK9 inhibitor, patients at high risk due to the presence of risk factors such as polyvascular disease, elevated LDL-C, diabetes, recurrent CV events, kidney disease or previous stroke (Fig. 4).

The last section requires information on the LDL-C levels achieved at 6 months to 1 year, and offers the opportunity to indicate which part of the local pathway should be refined or optimized, with the aim of further refining the application of the appropriate

approach with these patients (Fig. 5).

5. Report

This second part of the tool is a brief report allowing to position the results obtained in each single section with respect to either the latest European guidelines or other European countries (as an example of current practice) (Fig. 6). This will allow the physician to define the capability of the local pathway for the lipid management of ACS patients to follow these high CV risk patients with the most appropriate approach and to achieve the lipid goal defined for their CV risk category.

6. Next step

The last section allows physicians to suggest actions to be implemented in order to further optimize the management of ACS

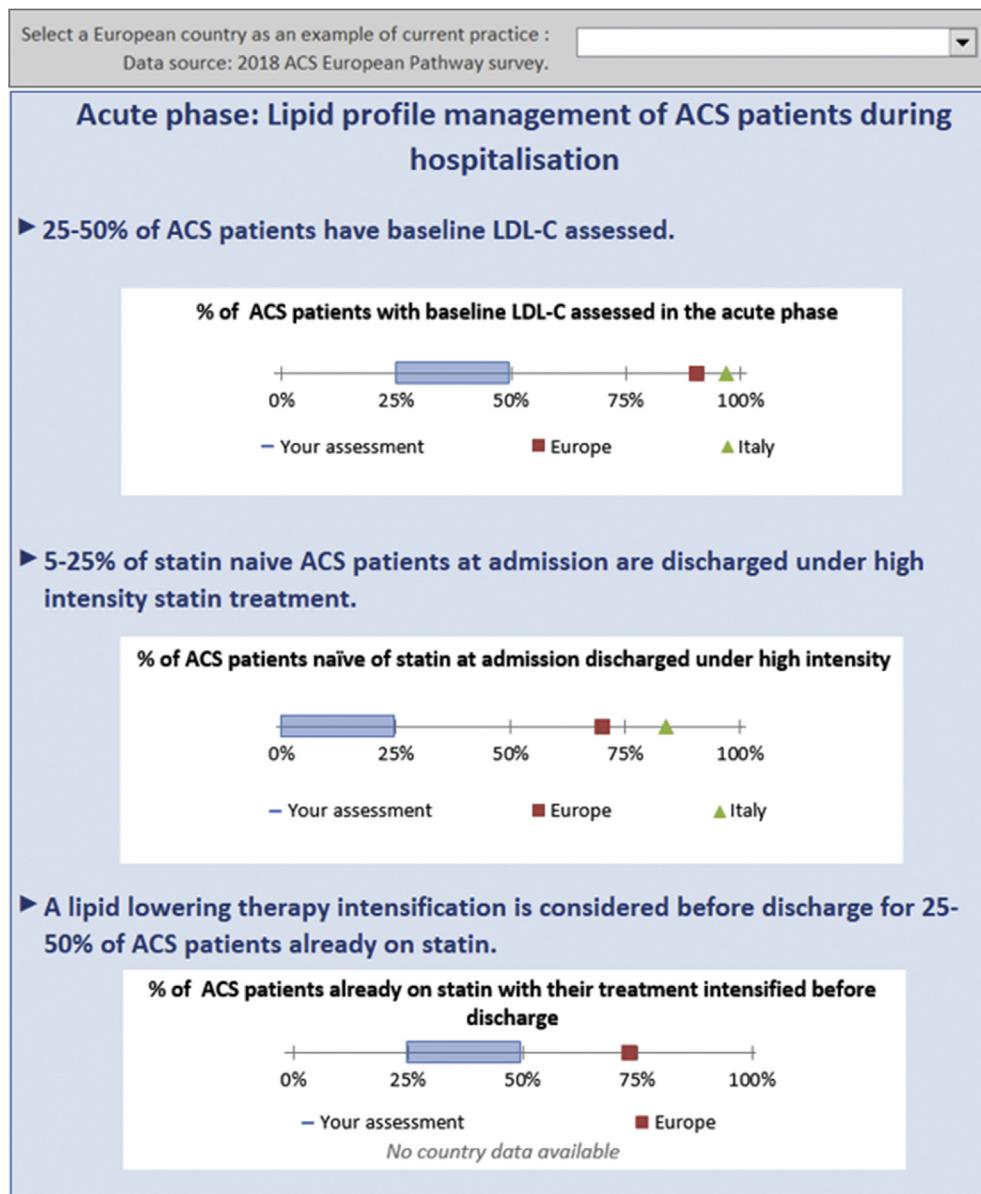


Fig. 6. Positioning of results with regards to other EU clinical practice stemming from the ACS Patient Pathway Project survey and the ESC/EAS Guidelines-An example.

patients.

Evaluation of the ACS Lipid EuroPath tool by practicing physicians revealed that 80% found the tool useful, and 74% found the tool easy to use; the possibility to compare clinical practice to the ACS EuroPath survey and to the dyslipidaemias guidelines was judged as positive by 75%.

7. Discussion

Post-ACS patients are at high risk of recurrent events and thus require a targeted pharmacological approach for optimal management of underlying risk factors. Hypercholesterolaemia represents a major risk factor in these patients, as several studies have shown that in clinical practice the achievement of the guidelines recommended LDL-C goal is obtained in a low percentage of patients (ref) [3,7]. This may be related to a broad range of factors; among them, the lack of common tools defining specific key steps for the management of patients with an ACS during the hospitalization (acute phase), at discharge, and at follow-up. The tool presented has been created with the aim to fill this gap, and to provide the physician with an instrument to optimize and improve lipid management in high CV risk patients. Furthermore, by comparing the results obtained by the physician with other examples of current practice would help define areas that can be potentially improved either at the individual or local level.

The development of this tool is based on the experience of previous studies. The ACS Patient Pathway Project (EuroPath I) survey was performed in 7 European countries with the aim of evaluating compliance to the recommendations from current ESC/EAS guidelines for the management of ACS patients and the effectiveness of secondary prevention in this high CV risk population [3]. The results showed that lipid management is still suboptimal despite the availability of highly effective lipid-lowering drugs, which exposes these patients to high risk of recurrent events. On the other hand, European initiatives in which local algorithms specific for ACS patients have been routinely applied successfully, translated into a significantly higher achievement of LDL-C goals due to the presence of lipid teams to which patients are referred to after discharge and the wide use of high intensity lipid-lowering therapies [4]. For these reasons, attention is drawn to the continuous evaluation of the lipid profile and lipid-lowering therapies at all stages (acute phase, discharge, and follow-up), as the benefits of statins in secondary prevention have been unequivocally demonstrated, and a large number of trials have shown the benefits of early and intensive statin therapy in ACS [6]. The relevance of the lipid-lowering approach in ACS patients has also been reviewed by the most recent ESC/EAS guidelines in which the addition of a PCSK9 inhibitor to current therapy is recommended when the LDL-C goal is not achieved after 4–6 weeks despite maximal tolerated statin therapy and ezetimibe [5].

Furthermore, there is emphasis on the importance of the role of screening for FH in ACS patients. In fact, although it is known that this inherited condition is common in the general population (~1:250) [8] and is even more common among ACS patients [9–13], several studies provided evidence that FH screening within ACS patient population remains largely unapplied. FH confers by itself a high- or very-high CV risk, and, due to the lifelong exposure to elevated levels of LDL-C, the occurrence of cardiovascular events at an early age compared with the general population must alert the cardiologist to start a specific pathway for the correct diagnosis and the appropriate pharmacological approach.

The intention is that application of this simple self-assessment tool will help bridge the guidelines to practice gap evident in the optimization of lipid management in ACS patients. To access the tool, please visit the page www.sitecs.it.

CRediT authorship contribution statement

Alessandro Sionis: Conceptualization, Methodology, Investigation, Supervision. **Alberico L. Catapano:** Conceptualization, Methodology, Investigation, Supervision. **Gaetano M. De Ferrari:** Conceptualization, Supervision, Methodology, Investigation. **Dariusz Dudek:** Conceptualization, Supervision, Methodology, Investigation. **J. Wouter Jukema:** Conceptualization, Supervision, Methodology, Investigation. **Angela Pirillo:** Writing - Original Draft, Writing - Review & Editing, Visualization. **François Schiele:** Conceptualization, Supervision, Methodology, Investigation. **Azfar Zaman:** Conceptualization, Supervision, Methodology, Investigation. **Jose L. Zamorano:** Conceptualization, Supervision, Methodology, Investigation.

Declaration of competing interest

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