

Organisational management of the time-dependent network for the treatment of acute coronary syndrome

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Parole chiave: Reti tempo-dipendenti; SCA; modello organizzativo

Abstract

Introduction. Cardiovascular diseases are the leading cause of death in Italy, being responsible for 227,350 deaths in 2020, according to the National Institute of Statistics. The implementation of timely reperfusion therapy is crucial to improve patient outcomes, and time-dependent networks for the treatment of Acute Coronary Syndrome, particularly ST-elevation myocardial infarction, have been established. In Tuscany, the network for the treatment of Acute Coronary Syndrome-ST-elevation myocardial infarction covers a vast area encompassing three Local Health Authorities, including all of South-Eastern Tuscany. Key features include equity of access, patient safety, improving the quality of care, standardization, the enhancement of professional skills, technological innovation, increasing case volumes and multi-professional integration across emergency services, hospital facilities and primary care networks. The Tuscan Acute Coronary Syndrome network provides comprehensive treatment for Acute Coronary Syndrome-ST-elevation myocardial infarction in 12 hospitals with 24-hour hemodynamics laboratories and has been extended to new territories, namely Piombino and the Island of Elba. The aim of the present study was to assess the impact of an analytical system for monitoring times to reperfusion treatment and subsequent actions, in order to improve the performance of the network.

Materials and Methods. In this retrospective study, we conducted an analytical evaluation of the network's performance, including reperfusion treatment times and factors causing delay. The study utilized data on patient transport, times from symptom onset to medical contact, and outcomes from the National Outcomes Program (NOP; "Programma Nazionale Esiti" in Italian). Analytical evaluations in 2021 measured the network's overall performance and identified the main causes of delay. The treatment process was divided into periods, from symptom onset to coronary reperfusion; interventions such as public awareness campaigns, electrocardiogram tele-transmission, and fast-track transfers were implemented in order to minimize delays.

Results. The lowest 30-day mortality rate in Acute Coronary Syndrome patients was recorded in hospitals that treated over 300

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cases annually, according to the 2020 and 2021 National Outcomes Program of. Improvements continued into 2022 and 2023, with mortality rates also declining in patients initially admitted to peripheral hospitals. Among residents of Piombino and the Island of Elba, 30-day mortality decreased from 8.8% (2017-2020) to 5.7% in 2022. In 2022, the Grosseto Hub treated 80% of ST-elevation myocardial infarction patients within 90 minutes.

Conclusions. The establishment of a well-organized time-dependent network for the treatment of Acute Coronary Syndrome-ST-elevation myocardial infarction in Tuscany significantly improved patient outcomes, thus demonstrating the critical role of timely and efficient care pathways. Our network's success is attributable to several factors, including improved accessibility, enhanced coordination among healthcare facilities, and the efficient use of technology and resources. These findings highlight the importance of structured clinical-care pathways in delivering high-quality care for Acute Coronary Syndrome patients.

Introduction

Background

The Tuscany Region has three Local Health Authorities (LHA): North-West, Center and South-East; these are territorial branches of the Regional Health Service and guarantee the homogeneity of health care in the various areas of the Region. The South-East Tuscany LHA (SET LHA) was created in 2016 from the merger of the previous smaller LHAs in the Provinces of Siena, Arezzo and Grosseto. The new LHA therefore includes 99 municipalities, 39 of which are mountainous, 20 are partially mountainous and one is an island.

The Siena University Hospital (SUH) is present in the territory of the SET LHA. Together, the SET LHA and the SUH constitute the so-called "Great South-East Area". The SUH is the reference hospital for this area, while 13 hospitals are under the direct management of the SET LHA, two of which (located in the cities of Arezzo and Grosseto) act as the reference hospitals for these two Provinces.

The area covered by the SET LHA is approximately 11,560 km², half of the entire Tuscany Region (approximately 22,990 km²). The population density is 70.36 inhabitants/km², less than half that of the Tuscany Region (159.36 inhabitants/km²). The demographic trend in this area is in line with the average regional values, with an increase in the proportion of elderly subjects over the years; residents over 65 years old now account for 27% of the total, while the so-called very elderly (over 85 years old) constitute 5%. Indeed, the trend in the aging index, has been steadily worsening for many years (+25% from 2011 to 2023), particularly in the Province of Grosseto, which includes some areas in which the aging index is much higher than the average of the LHAs: Colline

dell'Albegna (322.6), Amiata Grossetana (287.5) and Colline Metallifere (287).

In Italy, it is estimated that over 135,000 subjects per year are affected by coronary events, approximately 45,000 of which are fatal (1). As ACS is considered a time-dependent syndrome, it is essential to recognize its onset promptly and to intervene accordingly in order to reduce the risk of negative outcomes (2-6). However, it is also important to monitor patients appropriately after discharge and to provide adequate supportive and rehabilitation therapies (7).

Acute coronary syndromes (ACSs) encompass a spectrum of conditions that include recent changes in symptoms or clinical signs, with or without changes in the 12-lead electrocardiogram (ECG), and with or without acute elevations in blood concentrations of cardiac troponin (cTn) (5). Patients with suspected ACS may be diagnosed with acute myocardial infarction (AMI) or unstable angina (UA). ACS is associated with a wide range of clinical presentations, from the absence of current symptoms to ongoing chest complaints/symptoms, cardiac arrest, electrical/hemodynamic instability, or cardiogenic shock (CS) (8-9).

AMI is a term used to indicate a clinical event that is, in most cases, due to the formation of plaques in the internal walls of the arteries; the consequent decrease in blood flow results in a reduced supply of oxygen. The symptoms of AMI include chest pain extending from the left arm to the neck, shortness of breath, sweating, nausea, vomiting, abnormal heartbeat, anxiety, fatigue, weakness, stress, depression, etc.

Since the mortality or subsequent morbidity of ACS decreases drastically as the time between symptom onset and reperfusion is shortened, it is important to reduce any delay in treatment (10-11). Indeed, prompt effective treatment is essential to the survival of ACS patients, and early treatment has been clinically proved to reduce the mortality rate of acute

cardiac arrests, given that these crucial events occur within the first month in 30-50% of patients and, in up to half of these cases, within two hours, usually owing to ventricular fibrillation (11-12).

This high initial mortality appears to have changed little over the past 30 years; by contrast, there has been a marked reduction in mortality among patients treated in hospital. Indeed, from an average of 18% within 30 days in the mid-1980s, as revealed by a systematic review of mortality studies in the pre-thrombolytic era, the subsequent widespread use of fibrinolytic drugs, aspirin and coronary revascularization has reduced mortality to 6-7%, at least in large trials (13-15).

The aim of the present study was to assess the impact of a system of analytical monitoring of reperfusion treatment times and the consequent actions on improving the performance of the network.

A time-dependent network for the treatment of ACS-STEMI is effectively implemented throughout Tuscany (15-17). The network model takes into account the relevant legislation (8,15,18,19), the territorial organization and the resources currently available, and is based on the following key elements (8):

- equity of access;
- patient safety;
- improvement of the quality of care, including that of complex cases, in order to reduce mortality, disability and social costs;
- uniformity and standardization of the model;
- valorization of the professional skills of healthcare workers;
- innovation and adaptation of the network's technological resources;

- increasing the numbers of cases treated;
- integration among the local emergency network, the hospital network and primary care;
- organizational flexibility, multi-professional integration and inclusion.

The treatment of ACS-STEMI in Tuscany is provided by the STEMI network; this involves 12 hospitals with hemodynamic laboratories operating 24 hours a day, which are located throughout the Tuscany Region.

Materials and methods

The Grosseto hub of the ACS-STEMI network covers the entire territory of the Province of Grosseto. In addition, following an agreement between the North-West LHA and the South-East LHA, since 2021 the network has also included the Municipality of Piombino and the Island of Elba; the network therefore covers a total area of over 5,000 km² with 283,000 inhabitants, plus over 1,700,000 tourists/year during the summer. This area is the largest of the Tuscan provinces and has the lowest population density (Figure 1).

Many factors can delay reperfusion treatment in patients with ACS-STEMI, such as the time lag in alerting emergency services and dynamics that can influence the timing of the diagnosis itself and/or centralization of the patient.

In 2021, an analytical evaluation of the centralization pathways was carried out and reperfusion treatment times were monitored.



Figure 1 - Spoke centers and Grosseto hub.

SCHEDA PERCORSO STEMI

PAZIENTE:..... Inizio sintomi: data..... ora..... Chiamata: data..... ora.....

STEP 1 (FMC)

Prelievo sul territorio

Comune:.....

Pegaso ☐ Ambulanza ☐

ARRIVO PARTENZA

PS HUB (autopresentazione)

Sede:.....

Door in Door out

PS Spoke (autopresentazione)

Sede:.....

Door in Door out

Motivazione DI-DO>30min:

OPERATORE.....

PS ☐ 118 ☐

(STEP 2)

PS HUB (trasp. 2°)

Sede:.....

Door in Door out

PS Spoke (trasp. 2°)

Sede:.....

Door in Door out

Motivazione DI-DO>30min:

OPERATORE.....

PS ☐ Cardiologo ☐

(STEP 3)

PS HUB (trasp. 3°)

Sede:.....

Door in Door out

Motivazione DI-DO>30min:

OPERATORE.....

PS ☐ Cardiologo ☐

STEP 4

EMODINAMICA

ARRIVO

Si No

Coro: ☐ ☐

PCI: ☐ ☐

BALLOON

.....

Figure 2 - Form used to report transportation time.

Monitoring enabled the overall performance of the network to be measured and the main reasons for delay to be identified.

The treatment pathway of ACS-STEMI patients, from symptoms' onset to coronary reperfusion therapy, was subdivided into three main "periods": SO-FMC (symptoms' onset - first medical contact), which constitutes the time between the onset of symptoms and the first medical contact; FMC-HEMO (first medical contact - arrival to the hemodynamics

laboratory), which represents the time between the first medical contact and the patient's arrival in the hemodynamics laboratory; HEMO-BALLOON (arrival in the hemodynamics laboratory - reperfusion) which is the time between arrival to the hemodynamics laboratory and coronary reperfusion.

The main contributors to reperfusion time are reported in Figure 3.

The subanalysis of the components of the FMC-Balloon time is reported in Table 1.

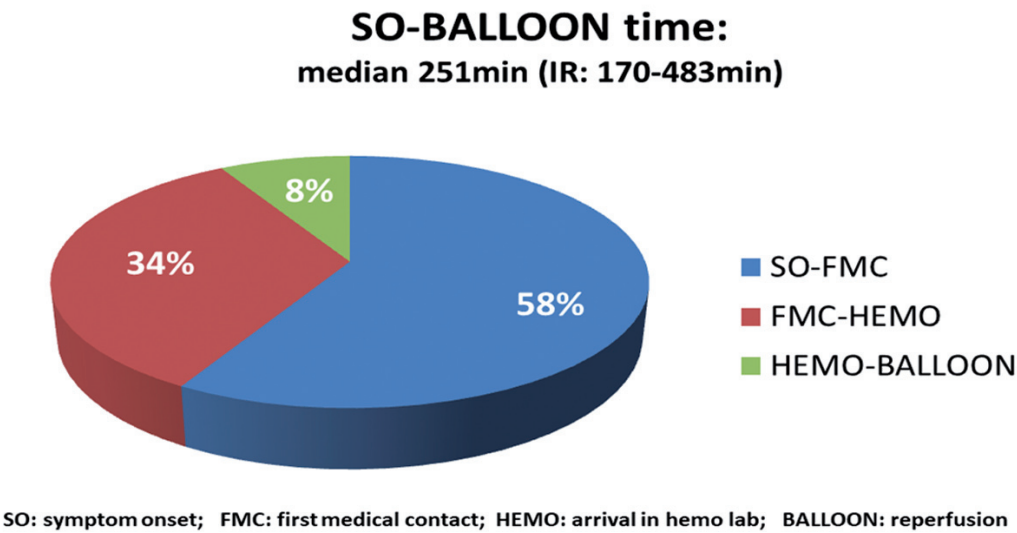


Figure 3 - Main contributors to reperfusion time.

Table 1 - FMC: first medical contact; HEMO: arrival into hemodynamics lab; BALLOON: reperfusion. *: $p < 0.05$ vs total monitored population. Time intervals expressed in minutes.

	Patients	FMC-HEMO	HEMO-BALLOON	FMC-BALLOON	FMC-BALLOON < 2h
	n (%)	Minutes median (IR 25 th -75 th)	Minutes median (IR 25 th -75 th)	Minutes median (IR 25 th -75 th)	%
All patients	150	105 (80-150)	33 (22-42)	140 (107-187)	36%
Self presentation:					
- All	69 (46%)	108 (75-151)	34 (25-44)	151 (108-185)	32%
- Admitted to Hub	15 (10%)	41 (29-62)	30 (20-35)	68 (59-124)	67%*
- Admitted to spokes	53 (35%)	121 (87-150)	36 (25-45)	157 (121-200)	23%
Home rescue:					
- All	81 (54%)	105 (60-150)	30 (21-38)	135 (110-182)	39%
- with Fast-Track	33 (22%)	85 (60-99)	30 (25-42)	115 (90-133)	60%*
- without Fast-Track	49 (33%)	130 (90-185)	28 (20-38)	167 (120-215)	24%
- Heli-ambulance	22 (15%)	141 (121-180)	35 (20-44)	181 (164-240)	5%*
- Ground-ambulance	67 (45%)	90 (77-135)	30 (21-39)	125 (103-175)	46%

Furthermore, a sub-analysis of reperfusion times was carried out according to the patient's method of presentation (118 emergency number or self-presentation), the means of transport used (ambulance or "Pegaso" air ambulance) and the possible implementation of the "fast-track" modality (17-19) (Figure 4).

The main causes of delays in treatment were discussed in a series of meetings and focus groups with the operators involved. It emerged that the implementation of an information campaign aimed at raising awareness among subjects with chest pain, instructing them to call the emergency number as soon as possible and to avoid self-presenting to the

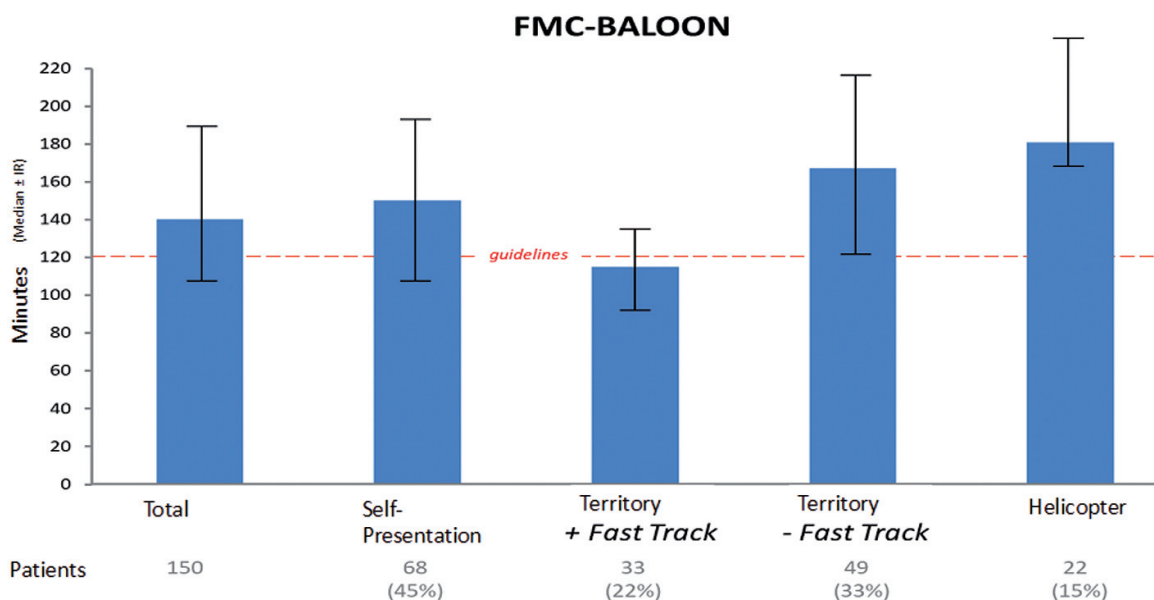


Figure 4 - Median times between first medical contact and reperfusion (FMC Balloon) according to the mode of presentation and transport.

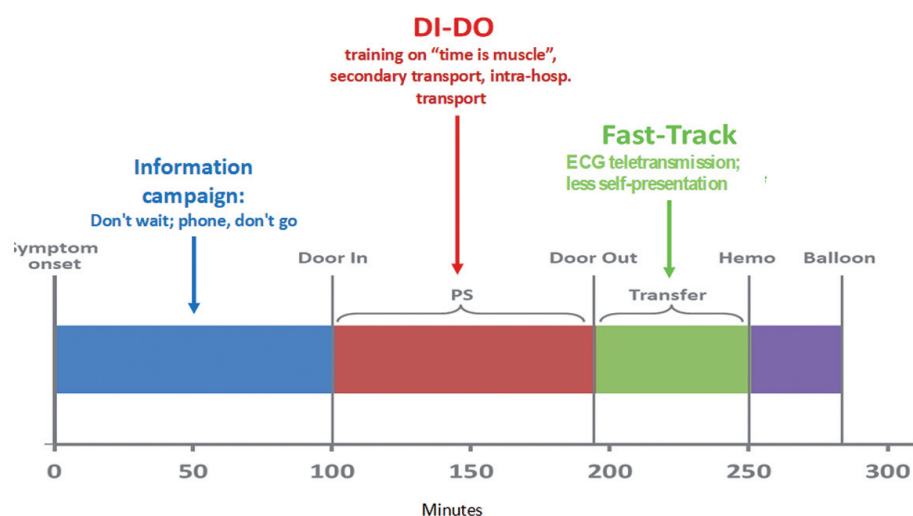


Figure 5 - Results of post-monitoring meetings. Main corrective maneuvers aimed at improving reperfusion times in patients with AMI. DI-DO (door in - door out): time from arrival to discharge at the first hospital.

emergency room reduced the average time lag between the onset of symptoms and the first medical contact, and favored rapid transfer to the hemodynamics lab.

The greater use of ECG tele-transmission before admission increased the use of rapid transfer of patients in the area. Moreover, transport by means of a dedicated ambulance enabled patients who self-presented to a spoke to be secondarily transported immediately to the reference hemodynamics department, thereby reducing overall treatment times.

The implementation of courses/seminars for emergency room medical/nursing staff, with the slogan: “il tempo è muscolo” (“time is muscle”) reduced delays due to the execution of diagnostic tests additional to the ECG, thereby accelerating centralization (Figure 5)

The National Outcomes Program (NOP; “PNE” in Italian) (20) is a National observatory of hospital care. By analyzing the variability of processes and outcomes between providers and between population groups, it monitors proven effective treatments and produces epidemiological evidence on the interactions among organizational structures, the modalities of care delivery and health services. The National Outcomes Program is run by in close collaboration with the Department of Epidemiology of the Lazio Regional Health Service, and the Istituto Superiore di Sanità (Higher Institute of Health) and, through the Regions and Autonomous Provinces, with the central institutions, the scientific community and the civil society.

To evaluate the efficiency of the Tuscan STEMI network, we analyzed the lethality at 30 days after ACS, which is considered a valid and reproducible indicator of the appropriateness and effectiveness of the diagnostic-therapeutic processes. An ACS episode was defined as any hospital admission occurring within 4 weeks of the date of the first ACS hospitalization. The numerator indicates the number of ACS episodes resulting in patient death within 30 days after the date of the first hospitalization for ACS; the denominator indicates the number of ACS episodes. The factors used for risk adjustment were: sex (also used in the stratified analysis), age and a range of comorbidities diagnosed during the first hospitalizations (within 28 days after the date of the first ACS), and during all hospitalizations in the previous 2 years.

According to the 2020 and 2021 NOP, the Grosseto Hospital recorded the lowest lethality rate among all Italian hospital facilities that treat at least 300 ACS/year. This figure is certainly the result of the good organization reached by the local network. In 2022 and 2023, after further interventions, the NOP data improved further in comparison with previous years. Indeed, the lowest lethality rate in Italy was recorded not only in patients on first admission to the Grosseto hub hospital but also among patients initially admitted to spoke hospitals throughout the rest of the province (Pitigliano, Castel del Piano, Orbetello, Massa Marittima) (Figure 6).

In STEMI patients living in Piombino and the Island of Elba, who were previously referred to the

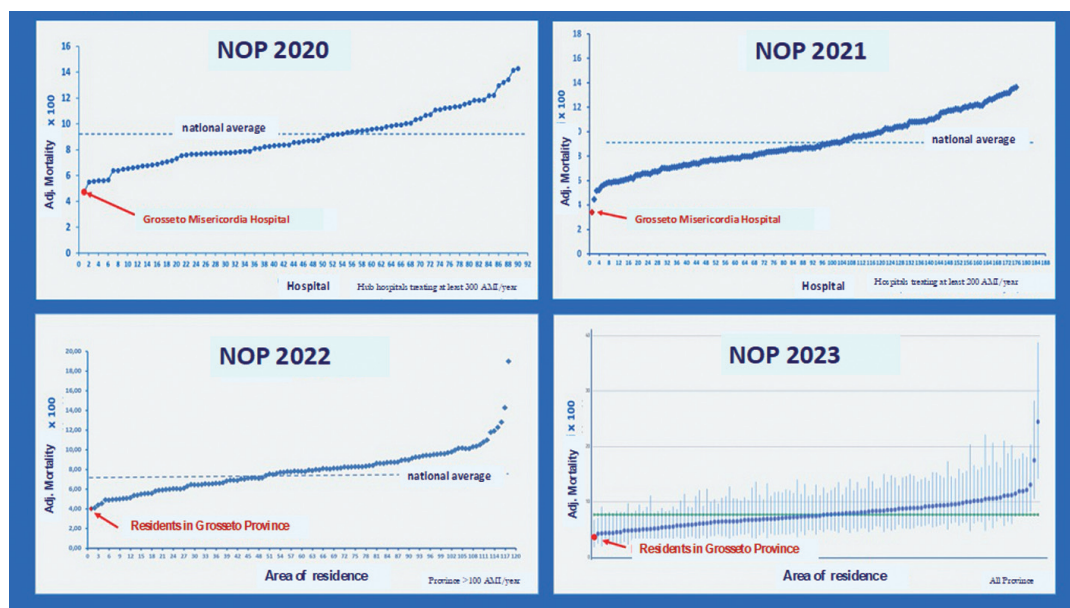


Figure 6 - 30-day lethality after AMI. NOP data 2020-2023.

Livorno hub (North-West LHA), and who have been referred to the Grosseto hub (SET LHA) since 2021, lethality at 30 days declined from 8.8% in the 2017-2020 period to 5.7% in 2022 (ARS-PROSE data, Ed. 2023), demonstrating correct integration of the new spokes into the new network (Figure 7).

The analytical monitoring project that was conducted in 2020-21 to assess the reaction times of the individual nodes referring to the Grosseto hub also favored the reduction of reperfusion treatment times. Indeed, regarding the activity carried out in the year 2022, 80% of STEMI patients referred to the Grosseto hub were treated within 90 minutes (ARS-PROSE data, Ed. 2023) (21), which constitutes the

best performance in Tuscany (Figure 8).

Moreover, among the LHAs in the Tuscany Region, the SET LHA recorded the highest percentage of PTCA performed for STEMI within 24 hours. Indeed, the Central LHA registered 72.5% of PTCA performed within 24 hours, the North-West LHA 74.2% and the South-East LHA 83.1% (19).

Discussion and Conclusions

According to the NOP, in the last four years the lowest mortality rate after hospitalization for ACS was observed in Grosseto and its province.

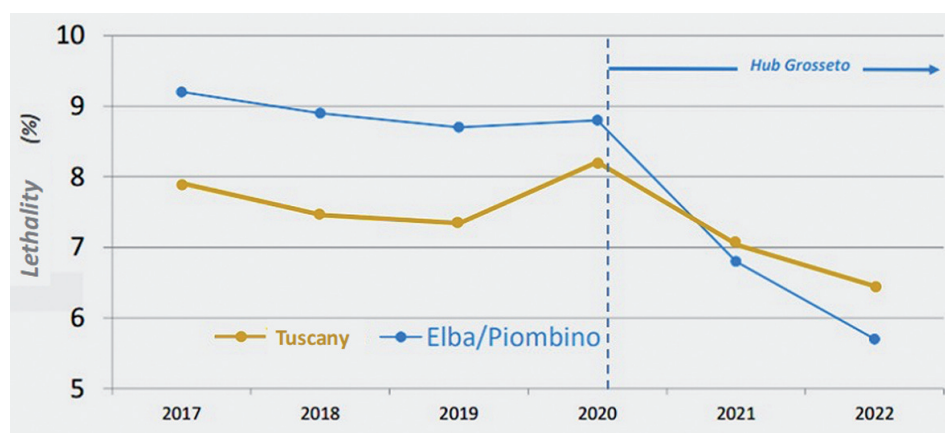


Figure 7 - AMI. lethality at 30 days, by residence.

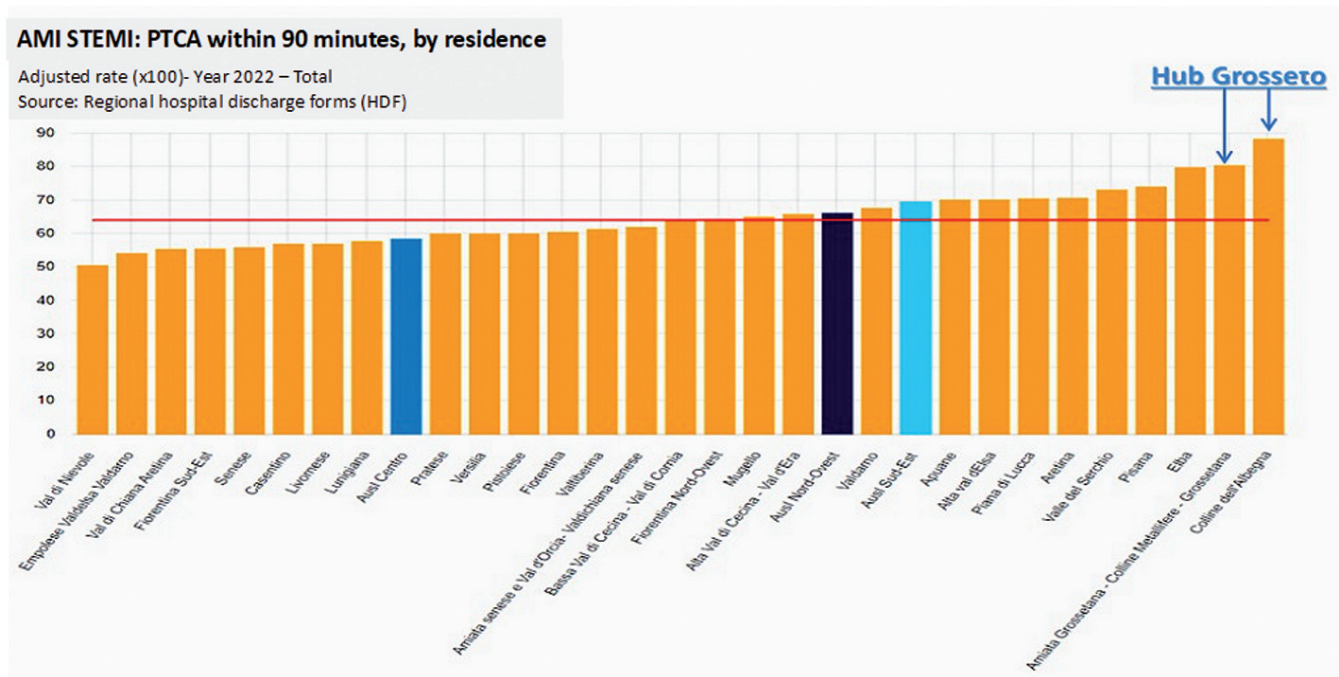


Figure 8 - AMI STEMI: PTCA within 90 minutes, by residence.

As mentioned above, time-dependent networks were established by Ministerial Decree 70/2015. However, in conformity with this decree, each Region subsequently implemented its own guidelines and operating methods. By 2020 and 2021, the Grosseto hospital had already recorded the lowest 30-day post-ACS lethality rate among all Italian hospital facilities.

In the two-year period 2022-2023, this record was further extended to all residents of the Province of Grosseto.

These results are attributable to the identification and improvement of the response times of the individual network nodes, not as a result of the analysis carried out on the use of ERs in rural and

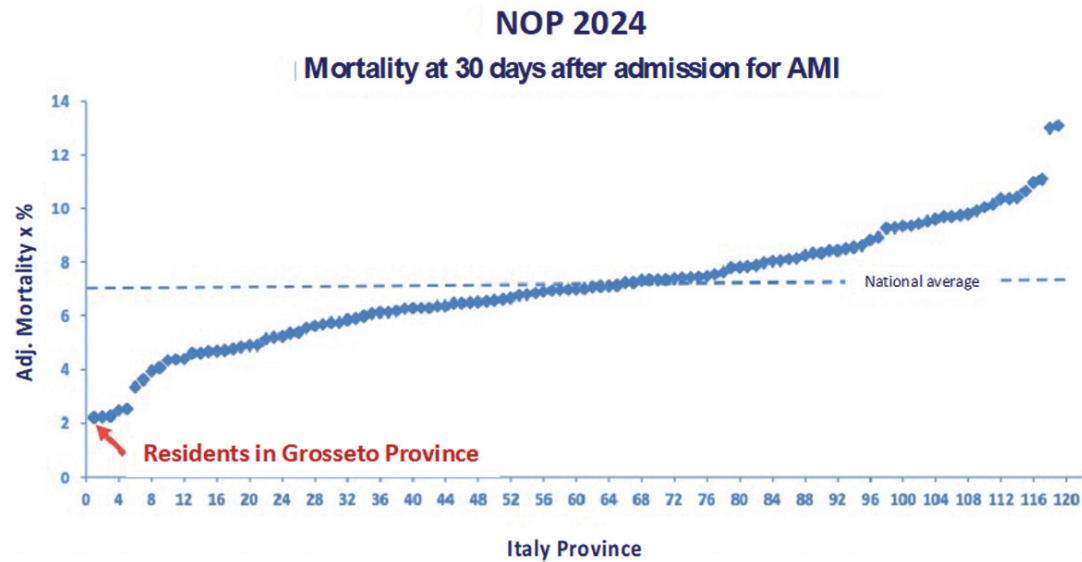


Figure 9 - 30-day lethality after AMI. PNE data 2024.

urban areas (22). In particular, this lower lethality has been achieved through the wider use of the fast-track approach, which reduces patient self-presentation and ensures faster transport from the spoke hospital to the hub, thereby reducing “door-in door-out” times. Indeed, reperfusion within 90 minutes was achieved in 73% of patients in 2018 and reached almost 82% in 2022. STEMI patients living in Piombino and on the Island of Elba have benefited from this improvement in lethality as can be seen from the results, which demonstrate the correct integration of the new spokes into the operational standards of the network (Figure 7).

Also for 2024, the adjusted lethality for Grosseto is the lowest in Italy (20) (Figure 9).

Conclusions

Efficient organization of clinical-care networks enables services to be provided at all levels. A well-organized network is characterized by effectiveness, clinical organization, appropriateness and efficiency in the use of resources. Structured clinical-care pathways have considerable repercussions on the quality of services provided in the areas of prevention, diagnosis and therapy.

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Conflicts of interest: The authors declare that they have no conflict of interest.

Ethics Approval: No ethics committee approval is required in Italy for epidemiological studies using health care administrative databases for research purposes and with individuals identified by an anonymous patient code. All methods were carried out in accordance with the Declaration of Helsinki.

Riassunto

La gestione organizzativa della rete tempo-dipendente per il trattamento della sindrome coronarica acuta

Introduzione. Le malattie cardiovascolari sono la principale causa di morte in Italia, essendo responsabili di 227.350 decessi nel 2020, secondo l'Istituto Nazionale di Statistica. L'attuazione di una terapia di riperfusione tempestiva è fondamentale per migliorare gli esiti dei pazienti e sono state istituite reti tempo-dipendenti per il trattamento della sindrome coronarica acuta, in particolare dell'infarto miocardico con sopraslivellamento ST. In Toscana, la rete per il trattamento della

sindrome coronarica acuta e dell'infarto miocardico con sopraslivellamento del tratto ST copre un'area vasta che comprende tre ASL, tra cui tutta la Toscana sud-orientale. Le caratteristiche principali sono l'equità di accesso, la sicurezza del paziente, il miglioramento della qualità dell'assistenza, la standardizzazione, la valorizzazione delle competenze professionali, l'innovazione tecnologica, l'aumento dei volumi dei casi e l'integrazione multiprofessionale tra i servizi di emergenza, le strutture ospedaliere e le reti di cure primarie. La rete toscana per la sindrome coronarica acuta fornisce un trattamento completo per la sindrome coronarica acuta con infarto del miocardio in fase ST in 12 ospedali con laboratori di emodinamica aperti 24 ore su 24 ed è stata estesa a nuovi territori, in particolare Piombino e l'Isola d'Elba. Lo scopo del presente studio è stato quello di valutare l'impatto di un sistema analitico per il monitoraggio dei tempi del trattamento di riperfusione e delle azioni successive, al fine di migliorare le prestazioni della rete.

Materiali e metodi. In questo studio retrospettivo, abbiamo condotto una valutazione analitica delle prestazioni della rete, compresi i tempi del trattamento di riperfusione e i fattori di ritardo. Lo studio ha utilizzato i dati sul trasporto dei pazienti, sui tempi dall'insorgenza dei sintomi al contatto con il medico e sugli esiti del Programma Nazionale Esiti (NOP). Le valutazioni analitiche del 2021 hanno misurato le prestazioni complessive della rete e identificato le principali cause di ritardo. Il processo di trattamento è stato suddiviso in periodi, dall'insorgenza dei sintomi alla riperfusione coronarica; per ridurre al minimo i ritardi sono stati attuati interventi come campagne di sensibilizzazione del pubblico, teletrasmissione di elettrocardiogrammi e trasferimenti rapidi.

Risultati. Il tasso più basso di mortalità a 30 giorni nei pazienti affetti da sindrome coronarica acuta è stato registrato negli ospedali che hanno trattato più di 300 casi all'anno, secondo il Programma Nazionale Esiti 2020 e 2021. I miglioramenti sono proseguiti nel 2022 e 2023, con tassi di mortalità in calo anche nei pazienti inizialmente ricoverati negli ospedali periferici. Tra i residenti di Piombino e dell'Isola d'Elba, la mortalità a 30 giorni è diminuita dall'8,8% (2017-2020) al 5,7% nel 2022. Nel 2022, l'hub di Grosseto ha trattato l'80% dei pazienti con infarto miocardico con sopraslivellamento ST entro 90 minuti.

Conclusioni. L'istituzione di una rete ben organizzata in funzione del tempo per il trattamento della sindrome coronarica acuta con infarto miocardico con sopraslivellamento del tratto ST in Toscana ha migliorato significativamente gli esiti dei pazienti, dimostrando così il ruolo critico di percorsi di cura tempestivi ed efficienti. Il successo della nostra rete è attribuibile a diversi fattori, tra cui una migliore accessibilità, un maggiore coordinamento tra le strutture sanitarie e un uso efficiente della tecnologia e delle risorse. Questi risultati evidenziano l'importanza di percorsi clinico-assistenziali strutturati per fornire cure di alta qualità ai pazienti affetti da sindrome coronarica acuta.

References

1. Perugini E, Maggioni AP, Bocanelli A, Di Pasquale G. Epidemiologia delle sindromi coronariche acute in Italia [Epidemiology of acute coronary syndromes in Italy]. *G Ital Cardiol (Rome)*. 2010 Oct;**11**(10):718-29. Italian. PMID: 21246773.
2. Jiang M, Mao J, Pu K, He B. Timing of early angiography in non-ST elevation acute coronary syndrome. *J Invasive*

- Cardiol. 2014 Feb;**26**(2):47-54. PMID: 24486660.
3. Deharo P, Bode C, Cohen M, Cohen M, Cuisset T, Mehta SR, et al. Timing of angiography and outcomes in high-risk patients with non-ST-segment-elevation myocardial infarction managed invasively: insights from the TAO trial (Treatment of Acute Coronary Syndrome with Otamixaban). *Circulation*. 2017 Nov 14;**136**(20):1895-907. doi: 10.1161/CIRCULATIONAHA.117.029779. Epub 2017 Sep 11. PMID: 28893843.
 4. Piironen M, Ukkola O, Huikuri H, Havulinna AS, Koukunen H, Mustonen J, et al. Trends in long-term prognosis after acute coronary syndrome. *Eur J Prev Cardiol*. 2017 Feb;**24**(3):274-80. doi: 10.1177/2047487316679522. Epub 2016 Nov 19. PMID: 27856805.
 5. Pell AC, Miller HC, Robertson CE, Fox KA. Effect of "fast track" admission for acute myocardial infarction on delay to thrombolysis. *BMJ*. 1992 Jan 11;**304**(6819):83-7. doi: 10.1136/bmj.304.6819.83. PMID: 1737145; PMCID: PMC1880988.
 6. Nante N, De Marco MF, Balzi D, Addari P, Buiatti E. Prediction of mortality for congestive heart failure patients: results from different wards of an Italian teaching hospital. *Eur J Epidemiol*. 2000;16(11):1017-21. doi: 10.1023/a:1010841102298. PMID: 11421469.
 7. Banerjee S, Rhoden WE. Fast-tracking of myocardial infarction by paramedics. *J R Coll Physicians Lond*. 1998 Jan-Feb;**32**(1):36-8. PMID: 9507439; PMCID: PMC9662960.
 8. Byrne RA, Rossello X, Coughlan JJ, Barbato E, Berry C, Chieffo A, et al; ESC Scientific Document Group. 2023 ESC Guidelines for the management of acute coronary syndromes. *Eur Heart J*. 2023 Oct 12;**44**(38):3720-3826. doi: 10.1093/eurheartj/ehad191. PMID: 3762265.
 9. Salari N, Morddarvanjoghi F, Abdolmaleki A, Rasoulpoor S, Khaleghi AA, Hezarkhani LA, et al. The global prevalence of myocardial infarction: a systematic review and meta-analysis. *BMC Cardiovasc Disord*. 2023 Apr 22;**23**(1):206. doi: 10.1186/s12872-023-03231-w. PMID: 37087452; PMCID: PMC10122825.
 10. Lu L, Liu M, Sun R, Zheng Y, Zhang P. Myocardial Infarction: Symptoms and Treatments. *Cell Biochem Biophys*. 2015 Jul;**72**(3):865-867. doi: 10.1007/s12013-015-0553-4. PMID: 25638347.
 11. Guerchicoff A, Brener SJ, Maehara A, Witzienbichler B, Fahy M, Xu K, et al. Impact of delay to reperfusion on reperfusion success, infarct size, and clinical outcomes in patients with ST-segment elevation myocardial infarction: the INFUSE-AMI trial (INFUSE-Anterior Myocardial Infarction). *JACC Cardiovasc Interv*. 2014 Jul;**7**(7):733-40. doi: 10.1016/j.jcin.2014.01.166. PMID: 25060015.
 12. Cannon CP, Brindis RG, Chaitman BR, Cohen DJ, Cross JT Jr, Drozda JP Jr, et al. 2013 ACCF/AHA key data elements and definitions for measuring the clinical management and outcomes of patients with acute coronary syndromes and coronary artery disease: a report of the American College of Cardiology Foundation/American Heart Association Task Force on Clinical Data Standards (Writing Committee to Develop Acute Coronary Syndromes and Coronary Artery Disease Clinical Data Standards). *Circulation*. 2013 Mar 5;**127**(9):1052-89. doi: 10.1161/CIR.0b013e3182831a11. Epub 2013 Jan 28. PMID: 23357718.
 13. Pignone M, Alberts MJ, Colwell JA, Cushman M, Inzucchi SE, Mukherjee D, et al. Aspirin for primary prevention cardiovascular events in people with diabetes: a position statement of the American Diabetes Association, a scientific statement of the American Heart Association, and an expert consensus document of the American College of Cardiology Foundation. *Circulation*. 2010 Jun 22;**121**(24):2694-701. doi: 10.1161/CIR.0b013e3181e3b133. Epub 2010 May 27. PMID: 20508178.
 14. Steg PG, Bonnefoy E, Chabaud S, Lapostolle F, Dubien PY, Cristofini P, et al; Comparison of Angioplasty and Prehospital Thrombolysis In acute Myocardial infarction (CAPTIM) Investigators. Impact of Time to Treatment on Mortality After Prehospital Fibrinolysis or Primary Angioplasty. Data From the CAPTIM Randomized Clinical Trial. *Circulation*. 2003 Dec 9;**108**(23):2851-2856. doi: 10.1161/01.CIR.0000103122.10021.F2. Epub 2003 Nov 17. PMID: 14623806.
 15. Decreto Ministeriale 2 aprile 2015, n. 70. Regolamento recante definizione degli standard qualitativi, strutturali, tecnologici e quantitativi relativi all'assistenza ospedaliera. GU 4 giugno 2015, n. 127. Available from: <https://www.camera.it/temiap/2016/09/23/OCD177-2353.pdf> [Last accessed: 2025 Feb 2].
 16. Accordo Stato-Regioni del 24 gennaio 2018. Linee guida per la revisione delle Reti cliniche – Le Reti Tempo – Dipendenti". Available from: http://archivio.statoregioni.it/Documenti/DOC_063280_P.%209%20%20CSR%20Atto%20Rep.%2014%20%2024gen2018.pdf [Last accessed: 2025 Feb 2].
 17. DGRT n. 958/2018. Linee di indirizzo per le reti cliniche regionali. - Allegato A. Available from: http://www301.regione.toscana.it/bancadati/atti/Contenuto.xml?id=5191345&nomeFile=Delibera_n.958_del_27-08-2018-Allegato-A [Last accessed: 2025 Feb 2].
 18. DGRT n. 1378/2016. Reti cliniche tempo dipendenti di cui al D. M. 70/2015. Approvazione linee di indirizzo per la realizzazione delle reti regionali. Available from: <http://www301.regione.toscana.it/bancadati/atti/DettaglioAttiG.xml?codprat=2016DG00000001704> [Last accessed: 2025 Feb 2].
 19. Regione Toscana, Italy. Linee di indirizzo regionali per le reti cliniche tempo-dipendenti- rete emergenze cardiologiche infarto miocardico acuto- organismo toscano governo clinico, decisione numero 42/2023 del 09/11/2023. Available from: https://www.regione.toscana.it/documents/10180/153838593/All+A+-+Decisione+42_Rete+Cardio.pdf/879f23ff-8da8-e2ed-9998-9ddcf20fe418?t=170081936659 [Last accessed: 2025 Feb 2].
 20. AGENAS. Programma Nazionale Esiti Agenzia Nazionale per i Servizi Sanitari Regionali. Available from: <https://pne.agenas.it/home> [Last accessed: 2025 Feb 2].
 21. Dati PROSE-ARS TOSCANA- IMA STEMI: PTCA entro

90 minuti- erogazione. Available from: https://www.ars.toscana.it/banche-dati/dettaglio_indicatore-2501-ima-stemi-ptca-2-g?provenienza=prosero_elenco_indicatori_sintesi&par_top_geografia=09062601&dettaglio=ric_anno_geo_prosero [Last accessed: 2025 Feb 2].

22. Ramacciani Iseman C, Salini C, Nante N. Differenze di

ricorso al pronto soccorso tra aree urbane e rurali: analisi retrospettiva nella Toscana meridionale [Emergency department overuse amongst urban and rural areas: a retrospective descriptive analysis in Southern Tuscany.]. *Recenti Prog Med.* 2023 Jan;**114**(1):802-814. Italian. doi: 10.1701/3939.39229. PMID: 36573532.

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