A PRACTICAL GUIDE FOR EUROPEAN STROKE ORGANIZATION (ESO) STROKE UNIT ACCREDITATION OF ACUTE STROKE-READY CLINICS IN GREECE

Apostolos Safouris MD^{1, 2, 3}, Jobst Rudolf MD⁴, Theodore Karapanayiotides MD⁵, Sotirios Giannopoulos MD², Maria Gryllia MD⁶, Argyro Kiamili MD⁷, Odysseas Kargiotis MD¹, Klearchos Psychogios MD^{1, 2}, Thomas Tegos MD⁸, Sofia Vassilopoulou MD⁹, Vasileios Tentolouris-Piperas MD⁹, Eleni Bakola MD², Lina Palaiodimou MD², Konstantinos Vadikolias MD¹⁰, Panayiotis Mitsias MD¹¹, Georgios Tsivgoulis, MD^{2,12}

- ¹ Stroke Unit, Metropolitan Hospital, Piraeus
- ² 2nd Department of Neurology, National & Kapodistrian University of Athens, School of Medicine, "Attikon" University Hospital, Athens
- ³ Aktios Rehabilitation Center, Koropi, Attica
- ⁴ Department of Neurology, Papageorgiou Hospital, Thessaloniki
- ⁵ 2nd Department of Neurology, AHEPA University Hospital, Aristotle University of Thessaloniki, School of Medicine, Thessaloniki
- ⁶ Department of Neurology, Athens General Hospital G. Gennimatas, Athens
- ⁷ Department of Neurology, "Korgialenio-Benakio" Hellenic Red Cross Hospital, Athens
- ⁸ 1st Department of Neurology, AHEPA University Hospital, Aristotle University of Thessaloniki, School of Medicine, Thessaloniki
- ⁹ 1st Department of Neurology, National and Kapodistrian University of Athens, Eginition Hospital, Athens
- ¹⁰ Department of Neurology, Democritus University of Thrace, School of Medicine, Alexandroupolis
- ¹¹ Department of Neurology Medical School, University of Crete, Heraklion, Crete
- ¹² Department of Neurology, The University of Tennessee Health Science Center, Memphis, Tennessee, United States of America

Abstract

Recent advances in acute ischemic stroke treatment have ended, in theory, the therapeutic nihilism towards stroke. In practice, implementation of approved treatments still lags in many European countries. European Stroke Organization (ESO) Stroke Unit accreditation process is the first step for improving the quality of stroke services. The process is simple and straightforward but users unaccustomed with quality procedures may be intimidated by the requested documentation. Moreover, high variation of health systems among European countries may further complicate the presentation of an acute stroke-ready center in a way to fit the definition of an ESO-accredited stroke unit. The present narrative review may help the interested stroke physicians formulate a comprehensive presentation of their center in order to facilitate accreditation of those acute stroke-ready centers that have established high standards of stroke care. Several free online resources concerning stroke education and accreditation will be provided. This document will also address specific characteristics of the stroke health services in Greece, highlighting suboptimal practices in the hope to initiate actions to promote adherence to ESO standards. Translating recent scientific advances into current stroke care in Greece is a major challenge for Greek stroke physicians and collaboration with public health agencies is necessary to achieve high quality care for stroke patients in Greece.

Key words: stroke, stroke units, accreditation, quality of care, European Stroke Organization, Greece



ΕΝΑΣ ΠΡΑΚΤΙΚΟΣ ΟΔΗΓΟΣ ΠΙΣΤΟΠΟΙΗΣΗΣ ΩΣ ΜΟΝΑΔΕΣ ΑΓΓΕΙΑΚΩΝ ΕΓΚΕΦΑΛΙΚΩΝ ΕΠΕΙΣΟΔΙΩΝ (ΑΕΕ) ΣΤΟΝ ΕΥΡΩΠΑΪΚΟ ΟΡΓΑΝΙΣΜΟ ΕΓΚΕΦΑΛΙΚΩΝ (EUROPEAN STROKE ORGANIZATION) ΤΩΝ ΕΛΛΗΝΙΚΩΝ ΚΛΙΝΙΚΩΝ ΠΟΥ ΝΟΣΗΛΕΥΟΥΝ ΟΞΕΑ ΑΕΕ

Σαφούρης Απόστολος^{1,2,3}, Rudolf Jobst⁴, Καραπαναγιωτίδης Θεόδωρος⁵, Γιαννόπουλος Σωτήριος², Γρύλλια Μαρία⁶, Κιαμίλη Αργυρώ⁷, Καργιώτης Οδυσσέας¹, Ψυχογιός Κλέαρχος^{1,2}, Τέγος Θωμάς⁸, Βασιλοπούλου Σοφία⁹, Τεντολούρης-Πιπεράς Βασίλειος⁹, Ελένη Μπακόλα², Λίνα Παλαιοδήμου², Βαδικόλιας Κωνσταντίνος¹⁰, Μήτσιας Παναγιώτης¹¹, Τσιβγούλης Γεώργιος^{2, 12}

- ¹ Μονάδα Εγκεφαλικών, Ιδιωτικό Θεραπευτήριο Metropolitan, Πειραιάs
- ² Β΄ Πανεπιστημιακή Νευρο*λογική Κλινική, Εθνικό Καποδιστριακό Πανεπιστ*ήμιο Αθηνών, ΠΓΝ «Αττικόν», Αθήνα
- ³ Κέντρο Αποκατάστασης «Άκτιος», Κορωπί Αττικής
- ⁴ Νευρολογική Κλινική, ΓΝ Παπαγεωργίου, Θεσσαλονίκη
- 5 Β΄ Νευρολογική Κλινική, ΠΓΝ ΑΧΕΠΑ, Αριστοτέλειο Πανεπιστήμιο Θεσσαλονίκης, Θεσσαλονίκη
- ⁶ Νευρο*λογική Κλινική, ΓΝΑ «Γ. Γενν*ηματάς», Αθήνα
- ⁷ Νευρο*λογική Κλινική, Γ.Ν.Α. «Κοργιαλένειο-Μπενάκειο Ελληνικό*ς Ερυθρός Σταυρός», Αθήνα
- 8 Α΄ Νευροπογική Κπινική, ΠΓΝ ΑΧΕΠΑ, Αριστοτέπειο Πανεπιστήμιο Θεσσαπονίκης, Θεσσαπονίκη
- ⁹ Α΄ Πανεπιστημιακή Νευρο*λογική Κλινική, Εθνικό Καποδιστριακό Παν*επιστήμιο Αθηνών, Αιγινήτειο Νοσοκομείο, Αθήνα
- 10 Νευρολογική Κλινική, Δημοκρίτειο Πανεπιστήμιο Θράκης, Ιατρική Σχολή, Αλεξανδρούπολη
- ¹¹ Νευρολογική Κλινική, Ιατρική Σχολή, Πανεπιστήμιο Κρήτης, Ηράκλειο
- ¹² Department of Neurology, The University of Tennessee Health Science Center, Memphis, Tennessee, United States of America

Περίληψη

Οι σύγχρονες εξελίξεις της θεραπευτικής του οξέος ισχαιμικού αγγειακού εγκεφαλικού επεισοδίου (ΑΕΕ) έθεσαν ένα τέλος στη μηδενιστική προσέγγιση των ΑΕΕ, τουλάχιστον θεωρητικά. Στην πράξη, η εφαρμογή των αποδεδειγμένων αποτελεσματικών θεραπειών υστερεί σε πολλές χώρες της Ευρώπης. Η διαδικασία πιστοποίησης μονάδων ΑΕΕ από τον Ευρωπαϊκό Οργανισμό Εγκεφαθικών (European Stroke Organization, ESO) δύναται να συμβάθει στη βεθτίωση της ποιότητας των υπηρεσιών υγείας για τους ασθενείς με ΑΕΕ. Η διαδικασία είναι απλή αλλά ιατροί ανεξοικείωτοι με διαδικασίες πιστοποίησης ίσως διστάσουν να προχωρήσουν σε αίτηση του κέντρου στο οποίο εργάζονται. Επιπθέον, διαφορές στην καθημέρα κλινική πρακτική μεταξύ Ευρωπαϊκών κρατών αυξάνουν την ανομοιογένεια και δυσχεραίνουν την παρουσίαση μιας κλινικής που νοσηθεύει ασθενείς με ΑΕΕ με τρόπο που να δείχνει προσαρμοσμένη στον ορισμό μιας μονάδας ΑΕΕ σύμφωνα με τον ESO. Η παρούσα περιγραφή στοχεύει να βοηθήσει τους ιατρούς που διαχειρίζονται ασθενείς με ΑΕΕ στο να δημιουργήσουν μια συνολική παρουσίαση της κλινικής τους, ώστε να ευοδωθεί η ευρωπαϊκή πιστοποίηση εκείνων των ελληνικών μονάδων που παρέχουν ήδη υψηλή ποιότητα υπηρεσιών στους ασθενείς με ΑΕΕ απλά παρουσιάζουν επάσσονες επλείψεις, που δεν είναι όμως απαγορευτικές της ευρωπαϊκής πιστοποίησης. Αναφέρονται ηθεκτρονικές πηγές εκπαίδευσης και πιστοποίησης με εθεύθερη πρόσβαση. Παρουσιάζονται συνοπτικά κάποια προβλήματα που αφορούν την επείγουσα διαχείριση ασθενών με ΑΕΕ στη χώρα μας με την ελπίδα να προωθηθεί ο διάλογος που θα οδηγήσει σε πρωτοβουλίες εναρμόνισης των κλινικών πρακτικών με τις ευρωπαϊκές κατευθυντήριες οδηγίες. Η μετάφραση των επιστημονικών επιτευγμάτων στην καθημέρα κλινική πρακτική διαχείρισης των ΑΕΕ στην Ελλάδα είναι η μεγάλη πρόκληση για τους ιατρούς που διαχειρίζονται ασθενείς με ΑΕΕ στη χώρα μας. Είναι αδήριτη ανάγκη η εμβάθυνση της συνεργασίας με τις αρχές δημόσιας υγείας της χώρας προκειμένου να επιτευχθεί υψηλή ποιότητα υπηρεσιών υγείας στους Έλληνες ασθενείς με ΑΕΕ.

Λέξειs ευρετηρίου: αγγειακό εγκεφαλικό επεισόδιο, μονάδες εγκεφαλικών, πιστοποίηση, ποιότητα υπηρεσιών υγείας, European Stroke Organization, Ελλάδα



Introduction

Randomized-controlled clinical trials have long solidified the crucial role of multidisciplinary stroke units for reducing post stroke mortality and disability [1]. Although organized services exist in most European countries, there is wide variability in the translation of treatment guidelines into clinical practice, and in adherence to quality indicators [2]. The European Stroke Organisation (ESO) in cooperation with the Stroke Alliance for Europe (SAFE) prepared a European Stroke Action Plan (ESAP) that included four overarching targets for 2030:

- 1. Reduce the absolute number of strokes in Europe by 10%.
- 2. Treat >90% of stroke patients in Europe in a dedicated stroke unit as the first level of care.
- 3. Create national plans for stroke encompassing the entire chain of care.
- 4. Fully implement national strategies for multisector public health interventions.

ESO has established certification processes for stroke units and stroke centers to improve quality and reduce discrepancies in stroke care, both within and between European countries [3]. Two levels of stroke care are certified:

Stroke units (SU): basic stroke care including IV thrombolysis, neuro-intensive care, diagnostics, secondary prevention, early treatment of complications and start of rehabilitation.

Stroke center (SC): a fully equipped institution, additionally providing endovascular treatment, advanced neuroimaging and surgical interventions.

There are 7 categories of main criteria for both SU and SC: (A) Lead, (B) Personnel, (C) General infrastructure, (D) Investigations, (E) Interventions and monitoring, (F) Teaching, meetings and research, (G) Numbers and quality indicators. Most decisive criteria are defined as **must** criteria that are considered essential and should be fulfilled completely. At least one of the leading physicians of the applying SU or SC needs to be an active member of the ESO. The application is provided in English but standard operational procedures (SOP) already in use in clinical practice are accepted in native language.

Greece has one of the highest incidences of firstever stroke in Europe (European Standard Populationadjusted incidence: 534.1 per 100 000 person-years) [4]. Although safety and efficacy of IVT and EVT have been demonstrated, their use is very limited (mean annual number of IVT in Europe: 142 per million inhabitants vs Greece: 20.5 per million inhabitants; 3.7 per million inhabitants EVTs in Greece vs. 37.1 per million inhabitants in European countries) [5-8]. Furthermore, the number of SU in both the public and private sector in Greece is limited, while only two SU have received ESO certification to date. In view of the former considerations, the present manuscript aims to serve as a practical guide for interested vascular neurologists to apply for accreditation, a process that offers multifaceted advantages for stroke clinics (Table 1). This document may serve as a roadmap for Greek vascular neurologists, stroke physicians and interventionists during the application process of their Stroke Unit Certification by ESO. A translation in Greek of main requirements is provided in the Appendix.

Stroke Unit Certification Process

A. Stroke Unit definition and multidisciplinary stroke teams

According to ESO, the definition of a stroke unit comprises the following elements: 1. A geographically dedicated clearly defined area or ward in a hospital: stroke unit beds are exclusively used for stroke patients. As such, they cannot be provided by the ICU on demand. This is a major point that troubles lowvolume centers that have difficulties acquiring stroke beds. Even if an ICU bed (with the corresponding ICU nurse) provides more advanced life support care, it cannot provide the expertise needed, as shown later in the definition. 2. Stroke patients are admitted and cared for by a multi-professional team (medical, nursing, and therapy staff) who have specialist knowledge of cerebral function, training and skills in stroke care with well-defined individual tasks, regular interaction with other disciplines, and stroke leadership.

In order to reach the ESO 2030 goal of admitting 90% of stroke patients in stroke units, currently available acute stroke-ready units need to be reinforced in Greece. Centralization of stroke care in one and only unit within each hospital will facilitate the creation of medical and nursing stroke care expertise and will allow the investment of resources for promoting stroke care to permit ESO SU accreditation in Greece. The recent governmental planning is to restructure hospital networks by distinguishing "hubs" that will offer advanced tertiary services and "spokes" that will treat most admissions but rapidly transfer complicated cases to hubs [11]. Stroke physicians should build on this initiative a whole country coverage map of stroke units and centers to diminish current regional variabilities in modern stroke care availability.

B. Personnel

B1. A stroke physician (at least a junior) is present at the institution around the clock 24/7. A stroke neurologist is available around the clock 24/7. The physical presence of a doctor trained in acute stroke is indispensable. Even though telestroke gained momentum during the current pandemic [12], ESO does not allow accreditation based on telestroke expertise. It is of



Table 1. Why should you apply for ESO certification?[9].

1.	Improve the quality of patient care by reducing variation in clinical processes. In the absence of national audits, ESO provides a unique opportunity in thrombolysis-ready stroke clinics to standardize treatment pathways and harmonize care with European standards.
2.	Provide a benchmark for quality of stroke management.
3.	Acquire an objective assessment of clinical excellence – ESO auditors have significant experience in stroke care, provide expert advice and follow well-defined criteria for evaluation based on the «European Stroke Organization recommendations to establish a stroke unit and stroke centre» [10].
4.	Creates a loyal, cohesive clinical team. The certification process provides an opportunity for staff to develop their skills and knowledge. The accreditation process involves all medical, nursing and paramedical personnel, all of which will contribute to the success of modern stroke care.
5.	Promotes a culture of excellence across the organization.
6.	Facilitates marketing, contracting and reimbursement. Promoting our work may strengthen our case for obtaining financial aid from non-profit organizations or resources from the public health system.
7.	Strengthens community confidence in the quality and safety of care, treatment and services. This is important for stroke units in the periphery.

note that stroke physician may be a junior doctor, even a physician during his specialty training and that even in non-neurology clinics, a stroke neurologist must be available around the clock, since neurological expertise may be needed in the differential diagnosis of stroke mimics or non-vascular neurological complications of acute stroke (eg seizures). The necessary documentation for B1 requirement includes "official and authorized Work plan and CV's of all stroke staff including full time equivalents". The work plan needs approval by the hospital authorities with names, official function, and signatures from two different persons. Training schedules, description of stroke training and integrations may be given in the local language.

B2. (Non-must criterion) A neurosonologist is available during regular working hours. Neurosonology expertise varies considerably among European countries. The ESO accreditation process does not require availability of a neurosonologist. Centers with availability of a neurosonologist should describe what is exactly provided and when during the day. It is possible that the widespread use of non-invasive angiography will further limit the role of neurosonology in the future.

B3. A radiology technician is present at the hospital around the clock, 24/7. A radiologist is present during official working hours and available 24/7. Neuroradiological or neurointerventional assistance by immediate dialogue (tele-stroke) is available 24/7 at the nearest stroke centre. Radiology technician physically present, radiologist during working hours and available 24/7 and neuroradiologist availability in a collaborating center are prerequisites for stroke unit accreditation. Despite allowing for the absence of a neuroradiologist, a signed agreement of collaboration by neuroradiologists / neuro-interventionalists at the stroke centre must be submitted, since challenging cases

may need specialist consultation at any given time.

B4. Cardiology expertise and internist expertise are available 24/7 or assistance by immediate call is available 24/7 at the nearest stroke centre. Cardiology and internal medicine specialists are needed in the work-up of stroke and for managing possible complications of stroke in the acute phase, but ESO allows for their absence in the hospital harboring the applicant unit, as long as a staff plan is submitted, with names of available specialists of cardiology and internal medicine available 24/7.

B5. (Non-must criterion) A specialist for neurorehabilitation is collaborating with the team. External collaborators may be accepted; physician's CV should be included in the application.

B6. Patients are cared by dedicated stroke trained nursing staff. There cannot be a stroke unit without stroke nurses. A series of documents need to be provided with every application: Training schedules for nurses, CV of the head-nurse of the SU, number of nursing personnel given in FTE (full time equivalent), and calculated number of nurse per bed/24hrs. The head nurse needs to show previous experience with stroke patients and should train any newcomer nurse to the basics of acute stroke nursing care. Recent advances in acute stroke treatment increase the responsibilities of nurses in the acute phase of stroke, as highlighted by the recent AHA guidelines [13].

Greece combines both the highest doctor-to-population ratio in the world and the lowest nurse-to-population ratio in Europe [14]. Consequently, nurses in Greece take charge of more patients but carry fewer responsibilities. This iatrocentric model of care means that treatment decisions are made by doctors, leaving only a very small opportunity for nurses to participate in the provision of multidisciplinary care [15]. Both trends are unacceptable for stroke care.



The role of stroke nurse cannot be overstated and each application to the ESO should clearly indicate the experience of the leading nurse and the accumulated experience of the stroke nursing team that needs to be adequate for the number of stroke beds.

There are several resources that may be available for nursing education in stroke. Nurses willing to deepen their knowledge in stroke care should be actively supported by stroke organizations which should invite trained nurses in their meetings. The MSc Stroke Program of the Medical School of Democritus University of Thrace accepts nurses with either a university, or a Technological Educational Institutes degree and it is currently the only way for a nurse to acquire an official certification in stroke medicine in Greece [16]. Online resources, albeit informal, are excellent to transmit the theoretical background. The ESO Angels' Initiative provides a full online certification comprising of 20 modules [17].

B7. Stroke trained physiotherapists (PTs) are part of the stroke team. B8. (Non-must criterion) Stroke trained occupational therapists (OTs) are part of the stroke team. In case of missing OTs, specify who is doing diagnostic testing of cognitive deficits. B9. Stroke trained speech, language and swallowing therapists (SLTs) are part of the stroke team. Rapid patient mobilization has been widely accepted as a means to hasten recovery in hospitalized stroke patients. Such an important task needs to be initiated, directed, and supervised by a trained physiotherapist that has previous experience with stroke patients. Also, part of the stroke nurse duties is to test all stroke patients for dysphagia on admission and initiate patient positioning but patients with difficulties in swallowing need assessment by a SLT that is also needed in the care of aphasic patients with prolonged hospitalization. The applicant needs to submit a detailed description of stroke training of PTs and SLTs as well as their names, FTE for PTs and SLTs as well as their numbers per stroke bed.

As described previously, the iatrocentric model of healthcare in Greece means that all paramedical specialties are underrepresented in Greek hospitals. Practically all ICUs in Greece have PTs [18], so in centers harboring an ICU, PTs in adequate numbers can also take care of stroke patients. Reported PT/ICU beds ratios range widely from 1:12 to 1:50, meaning that understaffed ICUs cannot possibly provide adequate personnel and this issue must be resolved before submitting the application. The situation is still worse with SLTs, as there will be many acute stroke-ready clinics in Greece that have no SLT coverage, especially in regional hospitals. However, this is a prerequisite for ESO accredited stroke care and incorporating external associates into the stroke team may be a solution to this problem, as long as a specialist with stroke background experience regularly visits the stroke unit and is accessible for emergencies during working hours. This must be thoroughly documented on submission.

OTs availability is not considered a must criterion. Whenever available, names of OTs, FTE for OTs and number of OTs per bed should be provided. If located outside the hospital, signed agreement and staff plan of OT expertise should be provided.

B10. (Non-must criterion) Support by social worker (SW) is available at the institution. When available, describe how SWs are integrated in the stroke team, provide names of SWs, FTE for patients, number of SWs per stroke bed. If located outside the hospital, provide a signed agreement and staff plan of SW expertise.

B11. (Non-must criterion) Patients get access to neuropsychologists. Specify who, when and where, is doing testing of cognitive function for stroke victims that are still active professionally / other similar challenges. Description of how neuropsychologists are integrated, names of neuropsychologists, FTE for patients, number of neuropsychological assessments of stroke patients during the previous year. If located outside the hospital, provide a signed agreement.

C. General Infrastructure

C1. Stroke patient care in a discrete area in the hospital, staffed by a specialist stroke multi-professional team with regular multi-professional meetings for planning care. For this purpose the Stroke Unit consists of a geographically defined stroke ward admitting stroke and TIA patients. This criterion is straightforward: Stroke beds are not to be shared with ICU, neurosurgery or other hospitalized patients. In the only systematic review comparing mobile stroke teams to geographically defined stroke units, no significant change in patient outcomes has been noticed [19]. However, the advantages of stroke wards have been outlined: better financial management, development of nursing expertise, facilitation of research, fundraising and volunteer support, as well as ease of implementation of guidelines and treatment protocols in clinical practice [20]. The applicant needs to submit a standard operating procedure (SOP): a document approved by the hospital authorities with names, official function and signatures from two separate individuals. SOP must include a plan of Stroke Unit facilities and a photograph of the monitoring unit/beds.

C2. The stroke unit is located in an institution that runs an emergency department (according to international standards, such as trauma level I or higher). C3 The stroke unit is located in an institution that runs an intensive care unit. Level 1 trauma centers are tertiary centers that include 24-hour availability of critical care coverage by all major medical specialties [21].



Emergency departments (ED) and ICUs complement the acute stroke care pathway and are indispensable to ensure continuity of care and immediate support of life-threatening stroke complications.

EDs have only recently been staffed with permanent medical personnel specialized in Emergency Medicine in Greece, while in most hospitals ED are properly staffed with trained nurses. Most physicians working in the ED are residents and attendees of different specialties that make rotating calls in the ED evaluating patients with symptoms related to their specialty. Another important consideration is the rotation in tertiary care hospitals covering medical emergencies in major urban areas in Greece. More specifically, the largest tertiary care hospitals in the capital of Greece, Athens, receive patients every four days according to the rotation system, while a similar rotation system has been implemented in Thessa-Ioniki (second largest city in Greece) and other large cities. This rotation system may represent a source of concern regarding the continuity of stroke care in Greece and should be explicitly explained to the ESO certification committee examining the application. In particular, it should be stated that no public hospital provides continuous emergency department availability in the regions of Attica and Thessaloniki. On the other hand, it should be noted that the total number of admitted stroke cases on an annual basis exceeds ESO demands (see below) since during active ED days the workload is exceedingly high.

C4. (Non-must criterion) The stroke unit runs an outpatient clinic for stroke and TIA patients. In case of absence of an outpatient clinic at your hospital, specify the type of follow-up of stroke care.

D. Investigations

D1. Emergency Computed tomography or magnetic resonance tomography are available 24/7 including imaging of cervical/intracranial vessels, access within 30 minutes for candidates of acute interventional therapy, Staff list, working plan, location plan in hospital – Access within 30 Min. provided. Time metrics are of outmost importance when presenting the information in the application related to this specific requirement. Reducing door to needle time to less than 20 minutes is feasible for standard, non-contrast CT-based intravenous thrombolysis. Meretoja et al [22] have summarized critical steps for bringing down door-toneedle times (Table 2) and we suggest implementing these steps using standard operating procedure (SOP) documentation in SUs applying for ESO certification. Furthermore, we suggest the implementation of a practical approach regarding neuroimaging for acute ischemic stroke patients with unknown time of stroke onset that are potential candidates for both on-label and off-label acute reperfusion therapies [24-25].

D2. Digital subtraction angiography (DSA) is available either in the own Stroke unit or within a nearby stroke centre SOP and in contact with a nearby stroke centre. Despite having lost some of its diagnostic indications to less invasive imaging modalities, interest in DSA has exponentially increased after the publication of the positive endovascular treatment randomized-controlled clinical trials. DSA availability is not prerequisite for SU application. However, collaboration with a nearby center that can proceed with DSA 24/7 has to be proven through appropriate documentation. This is an important point, since the ESO certification process for stroke units allows for the absence of endovascular treatment in place, but demands an established pathway for transfer to a thrombectomy-capable center. It should therefore made clear that no application without provision of endovascular treatment may be accepted, since the stroke treatment paradigm using only thrombolysis as recanalization therapy is harmful for large-vessel occlusion stroke patients.

In case there is no possibility for endovascular treatment in a center that is interested in applying for ESO certification then potential collaboration with the nearest stroke center with availability of angiography lab and neurointerventionalist may be explored in order to adopt a drip-and-ship paradigm. The SOP that will be submitted after being signed by all implicated parties, has to take into consideration estimated arrival times, the necessity or not of repeating imaging and, most importantly, availability, since many thrombectomy-ready centers lack resources to provide continuous service.

D3. Swallowing assessment is warranted 24/7, following a written procedure SOP. Dysphagia is very common in the acute stage of stroke and needs to be screened for by a stroke nurse on admission. Each center may develop its own protocol for dysphagia assessment, which should be completed for each patient. An example of a SOP in an ESO certified SU is presented in Figure 1 and a Greek translation in Supplementary Figure 1. The Angels Initiative provides free online course for oropharyngeal dysphagia pathophysiology and management [27], while the ESO recommendations for the diagnosis and treatment of post-stroke dysphagia offer additional insight on this critical issue of stroke management [28].

D4. Neurosonology assessment is available within 24 hours SOP. Neurosonology has been partially shadowed by the incorporation of vessel imaging in the ED for acute ischemic stroke patients (mostly using CT angiography) but it remains a valuable tool for vascular neurologists, allowing for easily repeatable, non-invasive, real-time brain hemodynamic assessment at the bedside [29-31]. Ultrasound assessment does not need to be available on admission, but availability within 24 hours of admission needs to be shown.



Table 2. Measures to reduce DNT, adapted from Meretoja et al. [22]

1.	Emergency medical services involvement to fast-track acute stroke patients
2.	Hospital prenotification to alarm the stroke team and preorder imaging studies and laboratory tests
3.	No-delay CT interpretation: Stroke physician interprets the CT scan, not waiting for formal radiology report. A stroke physician has to exclude two major things: intracranial hemorrhage and massive (more than a third of middle cerebral artery territory) brain hypodensity
4.	Premixing of alteplase with highly suspect thrombolysis candidates.
5.	Delivery of alteplase on CT table: Bolus administered on CT table but also continue alteplase infusion with intravenous drip.
6.	CT relocated to ED: Avoid elevators between ED and CT at all costs.
7.	CT priority: CT needs to be emptied prior to patient arrival so that the patient may be transferred directly onto CT table, not ED bed. This critical step highlights the importance of involving in the discussion radiologists and emergency department physicians.
8.	Rapid neurologic evaluation
9.	Preacquisition of history: a major hurdle that could be soon ameliorated with the planned introduction of electronic personal health records [23].
10.	Point-of-care international normalized ratio (INR): a low-cost solution that may deeply impact treatment and prognosis of patients on Vitamin K antagonists, suffering either from intracranial bleeding (permitting rapid reversal) or ischemic stroke with subtherapeutic (<1.7) INR (permitting thrombolysis).
11.	Reduced imaging for patients arriving <4.5h that can be thrombolysed on standard protocol.

D5. Investigations for establishing the aetiopathogenic diagnosis are available at the institution (Holtermonitoring at least for 24 hours, TTE, TEE, laboratory analysis, EEG). Stroke medicine has evolved through different clinical pathways and specialties in various countries, but neurology and cardiology expertise remain indispensable in every hospital harboring a SU.

E. Interventions and Monitoring (Native language permitted – review by national auditor only)

E1. (Non-must criterion) The stroke team establishes and follows written standard operating procedures (stroke pathways or written protocols, which should be revised regularly) for diagnosis, nursing, rehabilitation, prevention, follow-up, management of critical incidents. There is a concept for pediatric stroke, which defines and enables treatment/ management 24/7 in collaboration with the nearest stroke center or a pediatric competence center).

E2. (Non-must criterion) There are conceptual written protocols in relation to the emergency medical services, ED, and referring institutions. The concepts are revised regularly.

E3. (Non-must criterion) There are conceptual written protocols for all needs of rehabilitation.

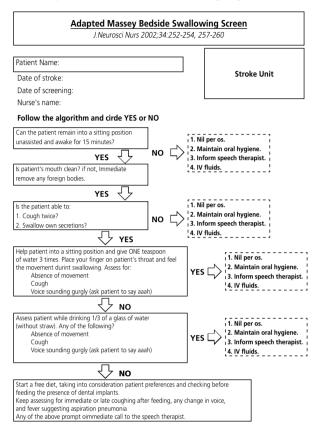
E4. (Non-must criterion) The stroke team establishes and works after a defined concept for swallowing disorders.

E5. IV-thrombolysis is available 24/7. Time from EMR arrival to thrombolysis (e.g. Door to needle time, complication rate) is assessed and documented. SOP Results of door to needle time and complication rate for the last year before application.

Applicant units should clearly present competence in thrombolysis through time metrics, to ensure timely and efficient recanalization therapy. The importance of documentation cannot be understated for the process of certification. The applicant center may opt for a retrospective analysis of time metrics, but it is strongly recommended to run a prospective registry of patients treated with thrombolysis for acute ischemic stroke. Even better, an electronic registry may be used to keep track of treatment rates, door to needle times and complication rates. The SITS-ISTR (Safe Implementation of Thrombolysis in Stroke -Thrombolysis Register) registry is a free online registry, already in use by Greek centers. SITS-ISTR was initially conceived for online documentation of acute ischemic stroke patients treated with intravenous thrombolysis in accordance with a study protocol, the SITS Monitoring Study (SITS-MOST) by the European Medicines Evaluation Agency. Currently SITS-ISTR has expanded to encompass data on ICH, atrial fibrillation and other aspects of acute stroke care [32]. SITS-ISTR registry has been endorsed by the ESO. The SITS-ISTR registry also serves a valuable resource to validate the quality of stroke care



Figure 1. An example of a nurse dysphagia screening SOP on admission of a stroke patient. Modified Massey Bedside Swallowing Screen [26], Greek translation. SOP or agreements or written protocols may be submitted in native language



both in individual centers and in Greece as a whole [6]. All European countries are registered, but reporting rates vary between countries; SITS registry has expanded to include countries from Asia, Africa and South America. In total, approximately 335,000 stroke patients from 1930 centers worldwide have been registered to SITS. In Greece, there are currently 29 active centers that have enrolled 2371 acute ischemic stroke patients treated with acute reperfusion therapies (10% mechanical thrombectomy, 90% intravenous thrombolysis).

Another important free online registry is the Res-Q (Registry of Stroke Care Quality) [33], initiated by the European Stroke Organisation- Enhancing and Accelerating Stroke Treatment (ESO East) Project to help both sites and countries improve their stroke care system. It was launched in May 2016 and targeted primarily the Eastern European countries [34]. It is designed to document the quality of stroke care through organized measurements that have been agreed by an international working group [35] and include the availability of stroke units, brain imaging, vascular imaging, cardiac arrhythmia detection, thrombolytic therapy, and other factors. Currently,

there are 20 active centers and 3590 acute stroke patients registered from Greece in Res-Q.

In the absence of a national stroke registry, all interested stroke physicians are strongly advised to take advantage of available free-to-use online registries as a tool for continuous monitoring, evaluation and improvement of health care quality in their center. Collaborative contribution will help identify gaps in health care delivery at a national, regional and hospital level. Participation in registries is not requisite for ESO accreditation. However, it facilitates any center's application by easily providing multiple metrics that are needed for accreditation and highlights the center's commitment in monitoring and improving quality of care. In view of these considerations, we strongly recommend joining either SITS-ISTR, RES-Q or both international registries before preparing the application for ESO SU certification.

E6. Neurosurgical and neurointerventional procedures are available 24/7 in collaboration with the nearest stroke center. Neurosurgical and neurointerventional expertise may not be available in the hospital harboring the stroke unit. However, a SOP must be in place to rapidly transfer acute stroke patients in need of neurointerventions (eg acute aneurysmal subarachnoid hemorrhage) to a collaborating stroke center.

E7. (Non-must criterion) Revascularization of the carotid artery with thrombendarterectomy or stenting is available in collaboration with a nearby stroke center 24/7. Similarly to neurosurgical and neurointerventional procedures, treatment of symptomatic carotid disease may not be available in place but must be promptly performed in eligible patients, in collaboration with a stroke center.

E8. The infrastructure of the stroke unit allows continuous monitoring of ECG, breathing, blood pressure, pulsoxymetry, and monitoring of glucose and temperature. Continuous monitoring allows for early detection and treatment of complications in the unstable subacute stroke patient: stroke in progression, cerebral oedema, epileptic seizures and non-cerebral complications [10].

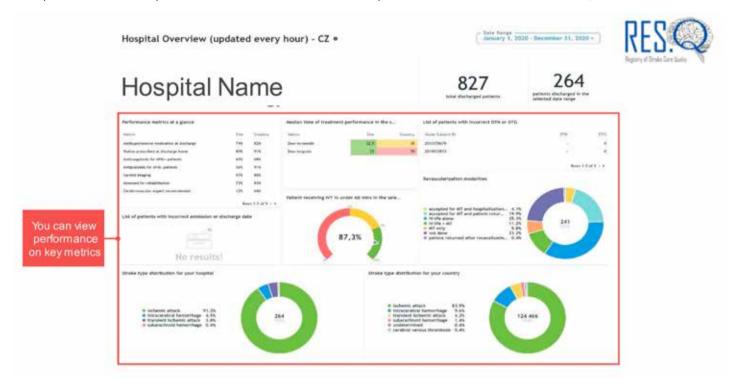
F. Teaching, Meetings, and Research

- F1. (Non-must criterion) Runs multidisciplinary group meetings at least once a week and documents in the chart proving that the case was discussed by the multiprofessional team.
- F2. (Non-must criterion) Organization of ongoing teaching courses and professional education for all groups represented in the stroke team (not only the doctors) is warranted and documented.
- F3. (Non-must criterion) Patients and their families should be regularly updated about treatment and prognosis.

The three aforementioned non-must criteria add



Figure 2. An example of Res-Q registry annual overview of a stroke unit. The registry's dashboard can be used to monitor performance and reports in excel can be downloaded. Adapted from "How to use RES-Q tool" [36].



value to any stroke unit and would be highly appreciated in any application.

G. Numbers and quality indicators

- G1. (Non-must criterion) The stroke unit has a stroke data base for quality control. Applicants should provide an annual report or online link or screen shot.
- G2. Minimal overall number of dedicated beds for stroke patients. Minimal number: 6. This number refers to both monitored and non-monitored beds.
- G3. (Non-must criterion) Minimal number of beds with automated monitoring. Minimal number: 4.
- G4. Minimal number of patients with TIA and acute stroke treated per year. Official and organized hospital statistics with percentages of different stroke types by annual report or database or online link; Minimum: 200. This number refers to both ischemic and hemorrhagic strokes.
- G5. (Non-must criterion) Numbers on acute treatment (IV-thrombolysis, door to needle time, type and rate of complications and number of referrals to acute intra-arterial interventions per year). Provide official and authorized hospital statistics by annual report or database with online link. Minimum IV-thrombolysis: 20. Also provide number of referrals for endovascular treatment.
- G6. (Non-must criterion) Documentation of age, sex, admission stroke severity case fatality, of discharge

- National Institutes of Health Stroke Scale, discharge modified Rankin Scale. Provide official and authorized hospital statistics by annual report or database with online link.
- G7. (Non-must criterion) Documentation of quality of stroke care: % documented swallowing test, early mobilization, and prevention of DVT. Provide relevant statistical data.
- G8. (Non-must criterion) Access to local stroke support organization.
- G9. Numbers of the relevant diagnostics (Number of TTE/TOE., Numbers of Neurovascular Ultrasound, Number of brain CT/MRI and CTA/MRA); Official and organized hospital statistics by annual report or database with online link.

All these metrics can be easily extracted by the RES-Q platform in case centers are actively participating in Res-Q (Figure 2). To the best of our knowledge there is currently no Greek hospital using an online local database dedicated to stroke patients. As a result, a retrospective review of patient files is needed to record all diagnostic examinations that have been performed by centers not yet participating in Res-Q. Finally, it should be mentioned that all applicants are strongly advised to start using online registries, since accreditation is a process to be repeated every 5 years and re-certification would be greatly facilitated when patient data is prospectively collected. This process represents a major advantage for a SU



applying for ESO accreditation: the process can be used as a means to further improve quality markers and advance quality of care.

Conclusions

The World Stroke Organization defines 3 levels of stroke care [37].

- 1. Minimum Healthcare Services: Care provided in local communities without coordination across defined geographic regions. Despite widespread availability of diagnostic studies and physicians, great variability persists in access to other healthcare workers (nurses, speech specialists) resulting in lack of basic training in swallow screens and dysphagia management in many Greek centers. The information in this manuscript does not refer to these centers since basic infrastructure is lacking to proceed to ESO SU accreditation.
- 2. <u>Essential Stroke Services</u>: Limited coordinated stroke care provided across geographically discrete regions. These clinics offer stroke expertise in medical and nursing personnel, a variety of diagnostic studies and acute intravenous thrombolysis. Many Greek clinics fulfill these criteria, and the current manuscript aims to help them proceed to the next level.
- 3. <u>Advanced Stroke Services</u>: Fully coordinated stroke care provided across geographically discrete regions. An ESO accredited stroke unit would fall in this category. There are currently only two low-volume private SU that have been accredited by ESO in Greece. Further inclusion of SU from public hospitals in ESO certification process is being incentivized and fully supported by National Scientific Societies including the Hellenic Society of Cerebrovascular Diseases and the Hellenic Neurological Society.

In conclusion, application for ESO SU certification process of Greek SUs will provide a benchmark that may assist the implementation of interventions that have been proven to advance the quality and efficiency of stroke care. It is also quite clear that in order to offer advanced stroke services to the entire Greek population and to align stroke care in Greece with European and international standards, it is not enough to create some low-volume centers of excellence, but Health Authorities need to address several long-standing fundamental issues concerning stroke care. The current iatrocentric model with rotational ED activation in major cities needs urgent update to accommodate modern stroke treatment paradigms. Communicating the need to restructure the current Health System is a task that exceeds our clinical work but deeply impacts it. Advocacy for stroke involves supporting stroke patients, building organizations, raising awareness and campaigning, but also working with, and influencing, decision makers.

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Appendix

Supplement 1 – Greek Translation of Main Requirements

A1. A dedicated geographically clearly defined area or ward in a hospital.

Αποκλειστική, σαφώς γεωγραφικά καθορισμένη περιοχή ή κλινική σε νοσοκομείο.

A2. Stroke patients are admitted and cared for by a multi-professional team (medical, nursing, and therapy staff) who have specialist knowledge of cerebral func-



tion, training and skills in stroke care with well-defined individual tasks, regular interaction with other disciplines, and stroke leadership.

Οι ασθενείς με Αγγειακά Εγκεφαλικά Επεισόδια (ΑΕΕ) εισάγονται και παρακολουθούνται από μία διεπιστημονική ομάδα (ιατροί, νοσηλευτές και θεραπευτές) με εξειδικευμένες γνώσεις των εγκεφαλικών λειτουργιών, εκπαίδευση και κατάρτιση στη φροντίδα του ΑΕΕ, με σαφώς καθορισμένες αρμοδιότητες, τακτική αλληλεπίδραση με άλλες ειδικότητες, και με ηγετικό ρόλο στην αντιμετώπιση των ΑΕΕ.

B1. A stroke physician (at least a junior) is present at the institution around the clock 24/7. A stroke neurologist is available around the clock 24/7.

Να είναι συνεχώς παρών ένας ιατρός με εμπειρία στα ΑΕΕ (έστω άρτι εκπαιδευμένος). Να είναι συνεχώς διαθέσιμος ένας αγγειακός νευρολόγος.

- B2. (Non-must criterion) A neurosonologist is available during regular working hours. (Προαιρετικό) Να υπάρχει διαθέσιμος νευροϋπερηχογραφιστής κατά τις εργάσιμες ημέρες και ώρες.
- B3. A radiology technician is present at the hospital around the clock, 24/7. A radiologist is present during official working hours and available 24/7. Neuroradiological or neurointerventional assistance by immediate dialogue (tele-stroke) is available 24/7 at the nearest stroke centre.

Να είναι συνεχώς παρών ένας τεχνολόγος ακτινολογικού στο νοσοκομείο. Να είναι παρών ένας ακτινολόγος κατά τις εργάσιμες ώρες, και να είναι συνεχώς διαθέσιμος. Να διατίθεται συνεχής νευροακτινολογική νευροεπεμβατική βοήθεια με άμεση επικοινωνία (tele-stroke) στο πλησιέστερο Κέντρο ΑΕΕ.

B4. Cardiology expertise and internist expertise are available 24/7 or assistance by immediate dialogue is available 24/7 at the nearest stroke centre.

Να υπάρχει διαθέσιμη συνεχής εξειδικευμένη καρδιολογική και παθολογική υποστήριξη ή αντίστοιχη βοήθεια με άμεση επικοινωνία στο πλησιέστερο Κέντρο ΑΕΕ.

B5. (Non-must criterion) A specialist for neurorehabilitation is collaborating with the team.

(Προαιρετικό) Η ομάδα να συνεργάζεται με ειδικό στην νευροαποκατάσταση.

B6. Patients are cared by dedicated stroke trained nursing staff.

Να παρέχεται νοσηλευτική φροντίδα στους ασθενείς από αποκλειστικό νοσηλευτικό προσωπικό, εκπαιδευμένο στα ΑΕΕ.

B7. Stroke trained physiotherapists (PTs) are part of the stroke team.

Na αποτελούν μέρος της ομάδας ΑΕΕ φυσιοθεραπευτές εκπαιδευμένοι στα ΑΕΕ.

B8. (Non-must criterion) Stroke trained occupational therapists (OTs) are part of the stroke team. In case of missing OTs, specify who is when doing diagnostic testing of cognitive deficits.

(Προαιρετικό) Να αποτελούν μέρος της ομάδας ΑΕΕ εργοθεραπευτές εκπαιδευμένοι στα ΑΕΕ. Σε περίπτωση απουσίας εργοθεραπευτών, να προσδιοριστεί ποιος διαγιγνώσκει τα νοητικά ελλείμματα.

B9. Stroke trained speech, language and swallowing therapists (SLTs) are part of the stroke team.

Na αποτελούν μέρος της ομάδας ΑΕΕ λογοθεραπευτές εκπαιδευμένοι στα ΑΕΕ.

B10. (Non-must criterion) Support by social worker (SW) is available at the institution.

(Προαιρετικό) Να υπάρχει υποστήριξη από κοινωνικούς λειτουργούς στο ίδρυμα.

B11. (Non-must criterion) Patients get access to neuropsychologists. Specify who is, when and where, doing testing of cognitive function for stroke victims that are still following their professional careers / other similar challenges.

(Προαιρετικό) Οι ασθενείς να έχουν πρόσβαση σε νευροψυχολόγους. Να προσδιορίζεται ποιος, που, και πότε διεξάγει νευροψυχολογικές δοκιμασίες στους ασθενείς με ΑΕΕ που εξακολουθούν να έχουν επαγγελματική δραστηριότητα ή άλλες παρόμοιες προκλήσεις.

C1. Stroke patient care in a discrete area in the hospital, staffed by a specialist stroke multi-professional team with regular multi-professional meetings for planning care. For this purpose the Stroke Unit dispose of an geographically defined stroke ward admitting stroke and TIA patients.

Η φροντίδα των ασθενών με ΑΕΕ να λαμβάνει χώρα σε διακριτή περιοχή του νοσοκομείου, στελεχωμένη από εξειδικευμένη διεπιστημονική ομάδα ΑΕΕ με τακτικές διεπιστημονικές συναντήσεις για τον προγραμματισμό της φροντίδας. Για αυτό το λόγο η Μονάδα ΑΕΕ να περιλαμβάνει μια γεωγραφικά καθορισμένη κλινική ΑΕΕ που δέχεται ασθενείς με ΑΕΕ και παροδικό ισχαιμικό επεισόδιο.

C2. The stroke unit is located in an institution that runs an emergency department (according to international standards, such as trauma level I or higher).

Η Μονάδα ΑΕΕ ανήκει σε ίδρυμα που διαθέτει Τμήμα Επειγόντων Περιστατικών (ανάθογο μονάδας τραύματος επιπέδου 1 σύμφωνα με τα διεθνή πρότυπα)

C3. The stroke unit is located in an institution that runs an intensive care unit.

Η Μονάδα ΑΕΕ ανήκει σε ίδρυμα που διαθέτει Μονάδα Εντατικής Θεραπείας.

C4. (Non-must criterion) The stroke unit runs an outpatient clinic for stroke and TIA patients.

D1. Emergency Computed tomography or magnetic resonance tomography are available 24/7 including imaging of cervical/intracranial vessels, access within 30 minutes for candidates of acute interventional therapy.

Να υπάρχει συνεχώς δυνατότητα επείγουσας αξο-



νικής ή μαγνητικής τομογραφίας, συμπεριθαμβανομένων απεικονίσεων τραχηθικών/ενδοκράνιων αγγείων, με πρόσβαση εντός 30 θεπτών για ασθενείς που είναι υποψήφιοι για επείγουσες παρεμβατικές θεραπείες.

D2. Digital subtraction angiography (DSA) is available either in the own Stroke unit or within a nearby stroke centre.

Na υπάρχει διαθεσιμότητα για ψηφιακή αγγειογραφία στην ίδια Μονάδα ΑΕΕ ή σε παρακείμενο Κέντρο ΑΕΕ.

D3. Swallowing assessment is warranted 24/7, following a written procedure.

Εξασφαλίζεται συνεχής δυνατότητα δοκιμασίας κατάποσης, βάσει γραπτού πρωτοκόλλου.

D4. Neurosonology assessment is available within 24 hours.

Υπάρχει διαθέσιμος νευροϋπερηχογραφικός έπεγχος εντός 24 ωρών.

D5. Investigations for establishing the aetiopathogenic diagnosis are available at the institution (Holtermonitoring at least for 24 hours, TTE, TEE, laboratory analysis, EEG).

Υπάρχει στο ίδρυμα δυνατότητα διενέργειας διαγνωστικών εξετάσεων για αιτιοπαθογενετική διάγνωση (Holter ρυθμού τουλάχιστον 24 ωρών, διαθωρακικό υπερηχογράφημα καρδιάς, διοισοφάγειο υπερηχογράφημα καρδιάς, εργαστηριακός έλεγχος, ηλεκτροεγκεφαλογράφημα).

E1. (Non-must criterion) The stroke team establishes and follows written standard operating procedures (stroke pathways or written protocols, which should be revised regularly) for diagnosis, nursing, rehabilitation, prevention, follow-up, management of critical incidents. There is a concept for pediatric stroke, which defines and enables treatment/ management 24/7 in collaboration with a at the nearest stroke center or a pediatric competence center).

(Προαιρετικό) Η ομάδα ΑΕΕ καθορίζει και να ακολουθεί γραπτώς διατυπωμένες τυποποιημένες διαδικασίες λειτουργίας (αλγόριθμος ΑΕΕ ή γραπτά πρωτόκολλα, που επικαιοροποιούνται τακτικά) για τη διάγνωση, τη νοσηλεία, την αποκατάσταση, την πρόληψη, την παρακολούθηση, και την αντιμετώπιση οξέων συμβαμάτων. Υπάρχει σχέδιο θεραπείας παιδιατρικού ΑΕΕ, που επιτρέπει και καθορίζει την αδιάκοπη αντιμετώπιση σε συνεργασία με το πλησιέστερο Κέντρο ΑΕΕ ή το αρμόδιο παιδιατρικό νοσοκομείο.

E2. (Non-must criterion) There are conceptual written protocols in relation to the emergency medical services, ED, and referring institutions. The concepts are revised regularly.

(Προαιρετικό) Υπάρχουν γραπτά πρωτόκολλα συνεργασίας με τις επείγουσες ιατρικές υπηρεσίες (ΕΚΑΒ), το Τμήμα Επειγόντων Περιστατικών (ΤΕΠ) και τα παραπέμποντα ιδρύματα. Τα πρωτόκολλα επικαιροποιούνται τακτικά.

E3. (Non-must criterion) There are conceptual written protocols for all needs of rehabilitation.

(Προαιρετικό) Να υπάρχουν γραπτώς διατυπωμένα πρωτόκολλα για όλες τις ανάγκες αποκατάστασης.

E4. (Non-must criterion) The stroke team establishes and works after a defined concept for swallowing disorders.

(Προαιρετικό). Η Ομάδα ΑΕΕ εφαρμόζει ένα προκαθορισμένο σχέδιο για τις διαταραχές κατάποσης.

E5. IV-thrombolysis is available 24/7. Time from EMR arrival to thrombolysis (e.g. Door to needle time, complication rate) is assessed and documented.

Υπάρχει αδιάκοπη δυνατότητα ενδοφλέβιας θρομβόλυσης. Μετράται και καταγράφεται ο χρόνος από την άφιξη μέχρι τη θρομβόλυση (χρόνος door-to-needle) καθώς και τα ποσοστά επιπλοκών.

E6. Neurosurgical and neurointerventional procedures are available 24/7 in collaboration with nearest stroke center.

Να υπάρχει αδιάκοπη δυνατότητα νευροχειρουργικών και νευροεπεμβατικών παρεμβάσεων σε συνεργασία με το πλησιέστερο Κέντρο ΑΕΕ.

E7. (Non-must criterion) Revascularisation of the carotid artery with thrombendarterectomy or stenting is available in collaboration with a nearby stroke center 24/7.

(Προαιρετικό) Υπάρχει αδιάκοπη δυνατότητα για επαναγγείωση έσω καρωτίδας με ενδαρτηρεκτομή ή τοποθέτηση ενδοπρόθεσης, σε συνεργασία με παρακείμενο Κέντρο ΑΕΕ.

E8. The infrastructure of the stroke unit allows continuous monitoring of ECG, breathing, blood pressure, pulsoxymetry, and monitoring of glucose and temperature.

Οι υποδομές της Μονάδας ΑΕΕ επιτρέπουν συνεχή παρακολούθηση ΗΚΓ, αναπνοών, αρτηριακής πίεσης, παλμικής οξυμετρίας, και απλή παρακολούθηση θερμοκρασίας και γλυκόζης αίματος.

F1. (Non-must criterion) Runs multidisciplinary group meetings at least once a week and documents in the chart that the case was discussed by the multiprofessional team.

(Προαιρετικό) Να διενεργούνται διεπιστημονικές συναντήσεις τουθάχιστον μία φορά την εβδομάδα όπου να συζητούνται τα περιστατικά, και να καταγράφεται αυτό στον φάκεθο κάθε ασθενούς.

F2. (Non-must criterion) Organizes ongoing teaching courses and professional education for all groups represented in the stroke team (not only the doctors) is warranted and documented

(Προαιρετικό) Οργανώνονται συνεχιζόμενα μαθήματα, εξασφαλίζεται και καταγράφεται η επαγγελματική εκπαίδευση για όλα τα μέλη που συγκροτούν την Ομάδα ΑΕΕ (όχι μόνο των ιατρών).

F3. (Non-must criterion) Patients and their families should be regularly updated about treatment and prognosis.

(Προαιρετικό) Οι ασθενείς και οι οικογένειές τους ενημερώνονται τακτικά για τη θεραπεία και την πρόγνωση.



G1. (Non-must criterion) The stroke unit has a stroke data base for quality control.

(Προαιρετικό) Η Μονάδα ΑΕΕ διατηρεί βάση δεδομένων ΑΕΕ για έλεγχο της ποιότητας.

G2. Minimal overall number of dedicated beds for stroke patients. Minimum: 6.

Ελάχιστος συνολικός αριθμός κλινών αποκλειστικά για ασθενείς με ΑΕΕ: 6.

G3. (Non-must criterion) Minimal number of beds with automated monitoring. Minimum: 4.

(Προαιρετικό) Ελάχιστος αριθμός κλινών με αυτόματη συνεχή καταγραφή: 4.

G4. Minimal number of patients with TIA and acute stroke treated per year. Minimum: 200.

Επάχιστος αριθμός ασθενών με παροδικό ισχαιμικό επεισόδιο και οξύ ΑΕΕ που αντιμετωπίζονται ανά έτος: 200.

G5. (Non-must criterion) Numbers of acute treatment (IV-thrombolysis, door to needle time, type and rate of complications and number of referrals to acute intra-arterial interventions per year).

(Προαιρετικό) Καταγράφεται ο αριθμός οξέων θεραπειών που διενεργούνται (ενδοφλέβια θρομβόλυση, χρόνος door-to-needle, είδος και ποσοστό επιπλοκών, και αριθμός παραπομπών προς οξείες ενδαρτηριακές παρεμβάσεις ανά έτος).

G6. (Non-must criterion) Documentation of age, sex, admission stroke severity case fatality, of discharge National Institutes of Health Stroke Scale, discharge modified Rankin Scale.

(Προαιρετικό) Καταγράφονται ηλικία, φύλο, βαρύτητα ΑΕΕ κατά την εισαγωγή, θνητότητα, NIHSS εξόδου, mRS εξόδου.

G7. (Non-must criterion) Documentation of quality of stroke care: % documented swallowing test, early mobilization, and prevention of DVT.

(Προαιρετικό) Καταγράφεται η ποιότητα της παρεχόμενης φροντίδας για το ΑΕΕ: % καταγεγραμμένων δοκιμασιών κατάποσης, πρώιμη κινητοποίηση, και πρόθηψη της εν τω βάθει φηεβικής θρόμβωσης.

G8. (Non-must criterion) Access to local stroke support organization.

(Προαιρετικό) Να υπάρχει πρόσβαση σε τοπικές οργανώσεις υποστήριξης ασθενών με ΑΕΕ.

G9. Number of the relevant diagnostics (Number of TTE/TOE., Numbers of Neurovascular Ultrasound, Number of brain CT/MRI and CTA/MRA).

Καταγράφεται ο αριθμός των σχετικών διαγνωστικών εξετάσεων που διενεργούνται (διαθωρακικά/ διοισοφάγεια υπερηχογραφήματα, νευροαγγειακά υπερηχογραφήματα, CT/MRI εγκεφάθου και CTA/MRA).

Supplementary Figure 1

