Clin Neuroradiol
https://doi.org/10.1007/s00062-019-00848-3

ORIGINAL ARTICLE

Endovascular Treatment Decision Making in Octogenarians and Nonagenarians

Insights from UNMASK EVT an International Multidisciplinary Study

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Received: 23 September 2019 / Accepted: 17 October 2019

Abstract

Background Evidence for efficacy and safety in stroke patients ≥80 years is limited, since they were underrepresented in randomized thrombectomy trials. This study sought to explore how physicians approach endovascular therapy (EVT) decision making in octogenarians and nonagenarians under their current local resources under assumed ideal conditions, i.e. without external (monetary or infrastructural) limitations.

Methods In an international multidisciplinary survey, 607 physicians involved in acute stroke care were randomly assigned 10 out of a pool of 22 case scenarios with different evidence levels for EVT, 4 of which involved octogenarians and 2 nonagenarians, and asked how they would treat the patient in the given scenario A) under their current local resources and B) under assumed ideal conditions, i.e. with no external restraints. Decision rates were calculated and clustered multivariable regression analysis performed to determine adjusted measures of effect size for patient age.

Results In octogenarians, physicians decided in favor of EVT in 76.7% (all of which were level 2B evidence scenarios) under current local resources and in 80.2% under assumed ideal conditions. In nonagenarians, 74.0% decided in favor of EVT under current local resources (level 1A scenarios: 87.7%, level 2B scenarios: 60.3%) and 79.2% would offer EVT under assumed ideal conditions (level 1A scenarios: 91.3%, level 2B scenarios: 67.2%). Age was not a significant predictor for treatment decision under current local resources (adjusted odds ratio, OR: 0.99, confidence interval, CI: 0.96–1.02 per decile increase) and under assumed ideal conditions (adjusted OR: 1.00, CI 0.97–1.03 per decile increase).

Electronic supplementary material The online version of this article (https://doi.org/10.1007/s00062-019-00848-3) contains supplementary material, which is available to authorized users.

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Published online: 08 November 2019

Conclusion The vast majority of physicians participating in this survey would offer EVT to acute ischemic stroke patients above 80 years.

Keywords Acute ischemic stroke · Elderly patients · Mechanical thrombectomy · Guidelines

Introduction

Endovascular therapy (EVT) is a highly effective treatment for acute ischemic stroke (AIS) due to large vessel occlusion (LVO) [1] and is now considered the standard of care [2]. In most randomized EVT trials, patients above 80 years of age were either excluded or underrepresented. The few available data on EVT in older patients show conflicting results: several small studies reported worse outcomes of octogenarians and nonagenarians following EVT [3–7] compared to younger patients. On the other hand, a recent meta-analysis by Sharobeam et al. showed that EVT in patients >80 years resulted in better outcomes compared to historical controls of the same age [7].

Old age per se is associated with a poorer prognosis after stroke, regardless of treatment [8, 9]. The reasons for this are manifold and include higher rates of comorbidities, withdrawal of care [10, 11], decreased neuronal plasticity [12] nutrition and available support [13]. In the HERMES (Highly effective reperfusion evaluated in multiple endovascular stroke trials) dataset, the rate of good outcomes for LVO patients above 80 years of age who did not receive EVT (control arm) was 14%, and the mortality rate 45% [1]. Currently, evidence regarding the benefit of EVT in older stroke patients is limited. High-level evidence is urgently needed, as the older AIS population is expected to increase due to an overall aging population. The best way to accurately determine efficacy, safety and cost-effectiveness of EVT in octogenarians and nonagenarians would be a randomized, controlled trial; however, such a trial would probably not be feasible, since it would be highly biased by the lack of clinical equipoise. In other words: most physicians will not be willing to randomize older patients with good baseline functional status while premorbid patients, who are less likely to benefit from EVT, will be more likely to get enrolled. To the best of our knowledge, there is currently no EVT trial for older stroke patients in planning. Thus, evidence for the benefit of EVT in patients >80 years will likely remain limited in the near future and EVT decisions mainly based on physicians' personal judgment.

This study aimed to explore how physicians approach endovascular therapy decision-making in octogenarians and nonagenarians under their current local resources and when assuming and ideal environment, i.e. without external (monetary, policy-related or infrastructural) limitations.

Methods

Survey Design

An international cross-sectional web-based survey (UNMASK-EVT) among stroke physicians was conducted to understand their current treatment practice and endovascular decision-making in acute stroke [14]. Participants were assigned to 10 out of a pool of 22 case scenarios and asked how they would treat the patient in the given scenario (EVT, intravenous alteplase, neither or both). Response data were obtained from 26 November 2017 to 27 March 2018. Approval by the local research ethics board was obtained.

Survey Participants

A total of 1330 stroke physicians (neurologists, interventional neuroradiologists, neurosurgeons, internists, geriatricians and other physicians directly involved in acute stroke care) from 38 countries were invited to participate in this web-based survey. No restrictions with respect to case volume or experience levels were applied and participants had both academic and nonacademic backgrounds. Prior to accessing the case scenarios, the physicians provided some personal data (age, gender, years of experience in stroke treatment, annual personal EVT and stroke treatment volume, annual center EVT and intravenous alteplase volumes, geographic region, subspecialty, hospital setting). Further details of the protocol were published elsewhere [14–16].

Clinical Case Scenarios

In this survey 22 case scenarios were designed to assess participants' treatment practice and particularly endovascular decision-making in acute stroke: 8 with level 1A evidence, 11 with level 2B evidence and 3 that were not covered by current American Heart Association/American Stroke Association (AHA/ASA) guidelines [14]. Of the scenarios four involved octogenarians (all of them with level 2B evidence for EVT) and two involved nonagenarians (one with level 1A and one with level 2B evidence for EVT). Participants were asked how they would treat the patient A) assuming there were no external (monetary or infrastructural) constraints, and B) given their local working conditions. For detailed descriptions of the six case scenarios involving older patients with their corresponding evidence levels see supplementary material.

Statistical Analysis

Survey data were analyzed using descriptive statistics; differences among subgroups were assessed with χ^2-tests and differences in the distribution of continuous measurements between groups were compared with Wilcoxon rank-sum tests. Multivariable stepwise logistic regression clustered by respondent was used to provide adjusted measurements of effect size for patient age. Adjustment was performed for physician and patient baseline characteristics (baseline Alberta Stroke Program Early CT Score (ASPECTS), time since symptom onset, patient age, site of occlusion, baseline functional status, level of evidence for EVT, physician age, gender, personal annual EVT and stroke treatment volume, annual center EVT and intravenous alteplase volumes, years of stroke treatment experience, hospital setting, specialty, region of practice). Odds ratios (OR) and 90% confidence intervals (CI) for continuous variables were reported per decile. *P*-values <0.05 were considered statistically significant. Data analysis was performed in Stata 15.1. Figures were created with Microsoft Power BI desktop 2016, Microsoft Corporation, Redmond, Washington, USA, and the Mapbox Visual Plugin.

Results

A total number of 607 physicians of different subspecialties (326 neurologists, 173 interventional neuroradiologists, 81 neurosurgeons, 27 physicians of other specialties) from 38 countries completed the survey and 6070 responses were obtained for the 22 case scenarios (1103 for octogenarian scenarios and 554 for nonagenarian scenarios).

Table 1 summarizes the decision rates in favor of EVT for the octogenarian and nonagenarian scenarios.

Overall current and ideal decision rates for patients above vs. below 80 years of age did not differ significantly ($p = 0.783$ and 0.270, respectively). Furthermore, overall EVT decision rates for octogenarian and nonagenarian scenarios did not differed under current local resources ($p = 0.227$) or under assumed ideal conditions ($p = 0.634$, Table 1). When looking at the responses for all 22 case scenarios, clustered multivariable regression analysis revealed that patient age was neither a predictor for the treatment decision under current local resources (adjusted OR 0.99, CI 0.96–1.02 per decile increase) nor for the decision under assumed ideal conditions (adjusted OR 1.00, CI 0.97–1.03 per decile increase).

The EVT decision rates for patients >80 years vastly varied among specialties (Fig. 1): current EVT decision rates ranged from 83.7% (neurosurgeons) to 64.0% (other specialties) and ideal rates from 82.7% (interventional neuroradiology) to 75.8% (neurosurgeons). The difference between current and ideal EVT rates was largest among physicians of other specialties (20.0%). Neurosurgeons' current EVT rate (83.7%) was higher than the ideal rate (75.8%). Specialty-specific EVT decision rates for octogenarians and nonagenarians are provided in the supplementary material.

Fig. 2 provides an overview about current and ideal EVT decision rates for patients >80 years of age in different countries and regions. Current EVT rates ranged from 82.9% (Middle East) to 57.1% (South Asia) and ideal rates from 81.9% (East Asia) to 77.1% (Middle East). Current EVT rates were remarkedly lower than ideal rates in South Asia (23.5% absolute difference) and South America (13.8% absolute difference), while in the Middle East, current EVT rates were higher than ideal rates (5.7% absolute difference).

Personal annual EVT volume (adjusted OR 1.09, CI 1.01–1.18 per decile increase), annual center EVT volume (OR 1.25, CI 1.13–1.37 per 10 case increase), annual center intravenous alteplase volume (OR 0.92, CI 0.86–0.98 per 10 case increase) and dependent baseline functional status (OR 0.25, CI 0.13–0.45) were significantly associated with current EVT decision in patients >80 years. Annual center EVT volume (OR 1.14, CI 1.04–1.25 per 10 case increase),

Table 1 EVT decision rates for octogenarian and nonagenarian case scenarios

Decision rate in favor of EVT	Level 1A evidence Scenarios	Level 2B evidence Scenarios	Total
Octogenarians (n = 1103)			
Current local resources—% (*n*)	–	76.7 (846)	*76.7 (846)*
Assumed ideal conditions—% (*n*)	–	80.2 (885)	*80.2 (885)*
Nonagenarians (n = 554)			
Current local resources—% (*n*)	87.7 (243)	60.3 (167)	*74.0 (410)*
Assumed ideal conditions—% (*n*)	91.3 (253)	67.2 (186)	*79.2 (439)*
All case scenarios (n = 5242)[a]			
Current local resources—% (*n*)	86.8 (1917)	66.3 (2011)	*75.6 (4586)*
Assumed ideal conditions—% (*n*)	90.6 (2001)	69.7 (2115)	*79.0 (4793)*

the values without brackets indicate percent, and the values in brackets the absolute number

EVT endovascular therapy

[a]The 3 scenarios without guideline recommendation for EVT, i.e. 828 responses, have not been included here

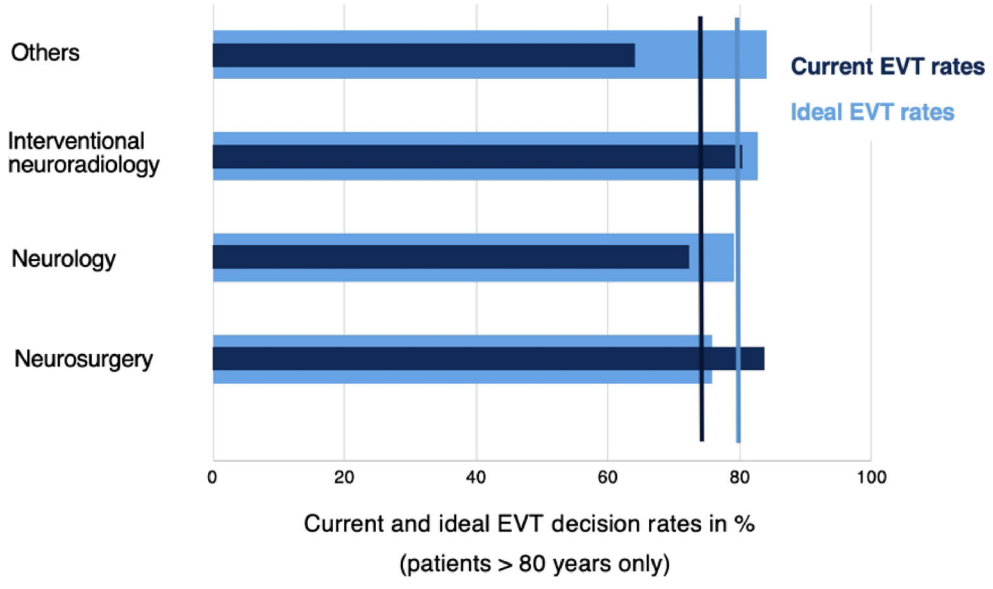

Fig. 1 Current and ideal decision rates in favor of endovascular therapy (EVT) in octogenarian and nonagenarians (in %) across different specialties. Dark bars represent current EVT decision rates and light bars ideal rates. Vertical lines represent overall average decision rates. Note that among neurosurgeons, current EVT rates were higher than ideal rates

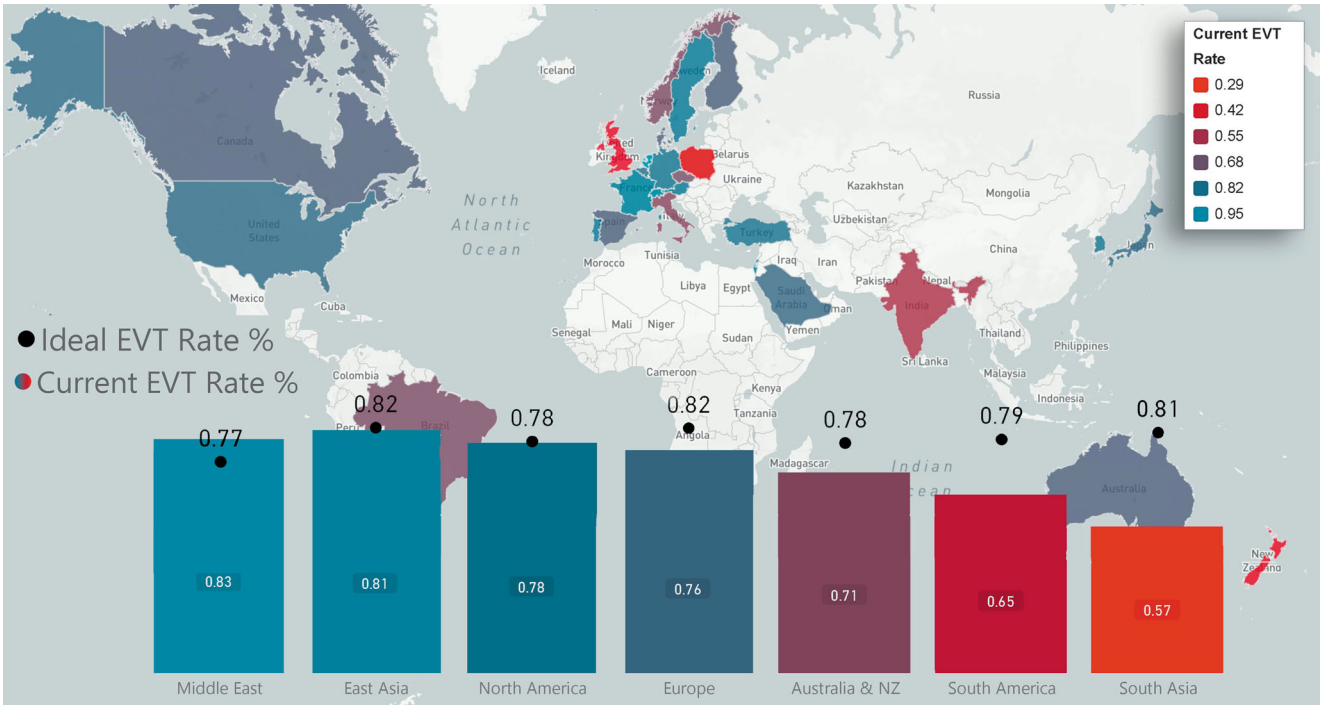

Fig. 2 Current and ideal decision rates in favor of endovascular therapy (EVT) for different geographic regions and countries. *Blue colored bars* indicate regions with high current EVT decision rates and *red colored bars* regions with low current EVT decision rates. Similarly, *blue colored areas* indicate countries with high current EVT decision rates and *red colored areas* countries with low current EVT decision rates. *Black dots* represent region-specific ideal EVT decision rates. Countries with less than 5 respondents have been omitted in this illustration

personal annual stroke volume (OR 0.89, CI 0.82–0.98 per 10 case increase), annual center intravenous alteplase volume (OR 0.92, CI 0.86–0.98 per 10 case increase), dependent baseline functional status (OR 0.20, CI 0.09–0.42), occlusion location (OR 0.59, CI 0.36–0.99) and the specialty neurosurgery (OR 0.47, CI 0.26–0.87, reference category neurology) were significantly associated with ideal EVT decision in this patient subgroup.

Discussion

In this international multidisciplinary survey, the vast majority of physicians would offer treatment to patients 80 years of age and older with EVT, and neither current nor ideal decision rates differed significantly between younger patients or octogenarians and nonagenarians. Age was not a significant predictor for treatment decisions under current

local resources or assumed ideal conditions. The results highlight a relatively aggressive treatment approach in this population, suggesting the lack of feasibility of a randomized controlled EVT trial in old people. The results are in line with current European [17] and North American [2] guidelines, both of which explicitly state that application of an upper age limit for EVT in AIS patients presenting within 6 h from onset is not justified. To the best of our knowledge, national guidelines of the countries represented in this survey either do not mention age as an eligibility criterion at all, or specifically state that age as a single factor should not be used as an exclusion criterion (e.g. German [18], French [19] and UK [20] guidelines).

Current and ideal decision rates varied remarkedly across specialties (Fig. 1): physicians of other specialties showed the largest difference between ideal and current EVT rates. They were in large parts geriatricians and internists and might often practice in smaller hospitals where 24/7 access to neuroendovascular treatment is limited, which could explain this difference. Among all specialties, neurosurgeons decided least frequently in favor of EVT under assumed ideal conditions and stated that they currently treat more octogenarians and nonagenarians with EVT than they would like to in an ideal environment and neurosurgery as a specialty significantly decreased the odds of a treatment decision in favor of EVT under assumed ideal conditions. Complications of EVT are more frequent in older patients, are associated with bad outcomes and often require neurosurgical intervention [4, 5]. Neurosurgeons frequently treat these complications in their daily routine and this could explain their more conservative management. While current EVT rates varied vastly among geographic regions, ideal rates were very similar and generally higher (77.1–81.9%): physicians seemed to agree in that EVT should be offered to older patients irrespective of their region of practice, but local conditions seemed to restrict their current decision to a different degree, with particularly severe external restraints in South Asia and South America (Fig. 2).

The only patient-related factors that were significantly associated to EVT decision-making were baseline functional status (both under current local resources and assumed ideal conditions) and occlusion site (under assumed ideal conditions only). This is not surprising, given the poor prognosis of patients with severe comorbidities and the higher degree of technical difficulty and risks for complications when performing EVT in distal (M2) occlusions. Higher personal and institutional EVT volumes were significantly associated with a current/ideal decision in favor of EVT. Complication rates of physicians and centers with higher caseloads were lower with improved outcomes [21, 22], and this might translate into a higher degree of treatment aggressiveness. High annual center intravenous alteplase volume and high personal stroke treatment volume were significantly associated with a current and/or ideal decision against EVT. The reasons for these findings require further research.

The study has several limitations: first, the overall response rate of physicians was modest with 45.6%. On the other hand, the response rate was higher than the commonly observed 20–25% in these studies. The number of responses for octogenarian and nonagenarian scenarios from certain geographic regions and specialties was low. Since there is no comprehensive international register of stroke physicians, participant enrolment was based on institutional networks and cooperations where participation was voluntary. The octogenarian/nonagenarian case scenarios included in this survey did not include patients with carotid-T or carotid-L occlusions (see supplementary material). These occlusions are different from "simple" M1/proximal M2 occlusions in the sense that they are more challenging to treat with EVT, and recanalization rates are lower [23]. It is possible that the survey participants might have decided in a different way had such scenarios been included. Thus, the results might not be generalizable to octogenarians and nonagenarians with T and L occlusions. Representativeness of the survey results can therefore not be unconditionally assumed. Survey data can only approach but never accurately depict decision-making in clinical routine; however, care was taken to design the case scenarios as realistic as possible and participants acknowledged that they reflected their clinical routine well. Despite its limitations, this study is a first step towards exploring physicians' endovascular treatment practice patterns in elderly AIS patients.

Conclusion

Most physicians participating in this survey decided to offer EVT to nonagenarians and octogenarians presenting with acute ischemic stroke. The results are in line with current European and North American guidelines, which do not consider old age a contraindication for EVT, despite the limited evidence for the efficacy and safety of EVT in this patient subgroup.

Acknowledgements The authors are most grateful to all participants of the survey.

Funding The study was funded by Stryker through an unrestricted research grant to the University of Calgary. The company was not involved in the design, execution, analysis, and interpretation or reporting of the results.

Compliance with ethical guidelines

Conflict of interest J.M. Ospel is supported by the University of Basel Research Foundation, the Julia Bangerter Rhyner Foundation and the

"Freiwillige Akademische Gesellschaft Basel" Foundation. U. Fischer is a consultant for Medtronic, Stryker and CSL Behring and Co-Principal Investigator of SWIFT-DIRECT, a randomized controlled endovascular stroke treatment trial (Medtronic). F. Turjman works as a consultant for Balt and Stryker. G. Saposnik is supported by the Heart and Stroke Foundation of Canada Career Award. M. Goyal is a consultant for Medtronic, Stryker, Microvention, GE Healthcare, Mentice. N. Kashani N, B. Menon, M. Almekhlafi, A. Wilson, B. Campbell, S. Yoshimura, M. Cherian, J.-H. Heo and M. Hill declare that they have no competing interests.

Ethical standards For this article no studies with human patients or animals were performed by any of the authors. All studies performed were in accordance with the ethical standards indicated in each case.

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