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Factors associated with the decision making on EVT

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Factors Associated With the Decision-Making on Endovascular Thrombectomy for the Management of Acute Ischemic Stroke

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Background and Purpose—Little is known about the real-life factors that clinicians use in selection of patients that would receive endovascular treatment (EVT) in the real world. We sought to determine patient, practitioner, and health system factors associated with therapeutic decisions around endovascular treatment.

Methods—We conducted a multinational cross-sectional web-based study comprising of 607 clinicians and interventionalists from 38 countries who are directly involved in acute stroke care. Participants were randomly allocated to 10 from a pool of 22 acute stroke case scenarios. Each case was classified as either Class I, Class II, or unknown evidence according to the current guidelines. We used logistic regression analysis applying weight of evidence approach. Main outcome measures were multilevel factors associated with EVT, adherence to current EVT guidelines, and practice gaps between current and ideal practice settings.

Results—Of the 1330 invited participants, 607 (45.6%) participants completed the study (53.7% neurologists, 28.5% neurointerventional radiologists, 17.8% other clinicians). The weighed evidence approach revealed that National Institutes of Health Stroke Scale (34.9%), level of evidence (30.2%), ASPECTS (Alberta Stroke Program Early CT Score) or ischemic core volume (22.4%), patient's age (21.6%), and clinicians' experience in EVT use (19.3%) are the most important factors for EVT decision. Of 2208 responses that met Class I evidence for EVT, 1917 (86.8%) were in favor of EVT. In case scenarios with no available guidelines, 1070 of 1380 (77.5%) responses favored EVT. Comparison between current and ideal practice settings revealed a small practice gap (941 of 6070 responses, 15.5%).

Conclusions—In this large multinational survey, stroke severity, guideline-based level of evidence, baseline brain imaging, patients' age and physicians' experience were the most relevant factors for EVT decision-making. The high agreement between responses and Class I guideline recommendations and high EVT use even when guidelines were not available reflect the real-world acceptance of EVT as standard of care in patients with disabling acute ischemic stroke. **(*Stroke*. 2019;50:00-00. DOI: 10.1161/STROKEAHA.119.025631.)**

Key Words: Acute ischemic stroke ■ endovascular therapy ■ thrombectomy ■ neuroeconomics ■ decision-making ■ evidence-based medicine ■ treatment guidelines

Several randomized controlled trials have proven the efficacy of endovascular thrombectomy (EVT) for patients with acute ischemic stroke because of a large intracranial vessel occlusion.[1–4] In addition, recent trials have confirmed the value of patient selection by imaging profile rather than time from onset.[5–7] Physicians now have a new, powerful, and

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effective therapeutic option to treat severe disabling strokes. However, they also face more complex decisions now (eg, drip-and-ship, prompt transfer to EVT center versus alteplase center, combined alteplase and EVT versus EVT alone for alteplase ineligible patients, etc).[8–10] Little is known about real-life factors that influence the selection of patients who receive EVT in daily practice

Patient selection for EVT may be influenced by multiple patient, physician, and systems factors and could vary across practitioners and healthcare systems. There are limited real-world data that facilitate our understanding of how physicians make therapeutic decisions.[11–15] Of importance, most physicians have limited structured training in risk management and decision-making.[16,17] Several studies have shown that treatment decisions are not infrequently unsupported by clinical trial data and influenced by multiple physician biases.[18,19]

In behavioral economics, uncertainty is a term that comprises both risk and ambiguity. Risk applies to events with known probability.[20] Ambiguity is a term reserved for events for which probabilities are unknown.[20] Typically, people are averse to both ambiguity and risk, and the 2 aversions are independent of each other.[21] Uncertainty is one of the most important contributing factors affecting decisions in medical care.[22,23] Key decision points in acute stroke include: time from symptoms onset to the diagnosis, therapeutic approach (eg, intravenous thrombolysis, EVT, both), transfer to tertiary stroke center, management of unexpected situations (eg, re-imaging in case of delays, new diagnosis of cancer, or history of preexisting dependency). Decisions based on erroneous assessments may result in unrealistic patient and family expectations and potentially suboptimal advice, treatment, and patient outcome. Our objective was to determine factors associated with the selection of patients for endovascular treatment to better understand the factors that influence these treatment decisions. We also examined the influence of tolerance to uncertainty on the decision to proceed with EVT and sought to determine practitioners' agreement with current guidelines when providing care in the acute setting.

Methods

Design and Participants

We conducted a web-based question survey using the Qualtrics Data Collection and Analytics platform (www.Qualtrics.com). The study comprised of the following 3 phases: (1) demographic and practice information, (2) behavioral battery from standardized surveys and 4 experiments to assess physicians' risk preferences, (3) case scenarios. Participants were randomized to 10 of 22 case scenarios, which were designed to address the choice of EVT both when supported by multisocietal and multinational guidelines and when no specific recommendations were available.[4,24–27] Survey respondents were physicians of different specialties (eg, neurologists, stroke neurologists, interventional radiologists, or neurosurgeons with expertise in EVT) directly involved in acute stroke care decisions from 38 countries that were recruited by designated country principal investigators from Nov 6, 2017 to April 29, 2018. We allowed the participation of general internists or geriatricians as in some countries (eg, United Kingdom) and they are responsible for providing acute stroke care. Responders were invited to participate by one of the country principal investigators. All participants received compensation for completing the survey. The study was approved by the Research Ethics Board at the University of Calgary, Canada.

As a result, those participants were included in our study.

Behavioral Battery

We included behavioral experiments to assess participants' risk preferences and tolerance to uncertainty.[28,29] In brief, ambiguity aversion is defined as dislike for events with unknown probability compared with events with known probability.[28] In the medical domain, an ambiguity-averse individual would rather choose a treatment where the probability of benefits or side effects is known (even if these are somewhat unfavorable) over one where this probability is unknown (see Figure I in the online-only Data Supplement). Risk experiments involved determining the subjective value of a risky (50/50) option instead of a safe (100%) option. Participants were asked what the minimal certain payoff would be (safe option) that they would prefer over the equiprobable gamble (50/50 option) of winning 400 or 0 US$ (expected value of 200 US$).

We used 2 standardized surveys to assess physicians' willingness to take risks and tolerance to uncertainty; the German Socio-Economic Panel, which evaluates willingness to take risks in different (financial, health, etc) domains,[30] and the reaction to uncertainty test,[31] which gives a total score from 5 questions.[32] Low tolerance to uncertainty was defined as values below the median of the total score. Details have been published in previous studies and in the online-only Data Supplement.[33]

Definitions

For the primary analysis, we classified the 22 case scenarios according to the current treatment guidelines.[4,24,26,27] Eight case scenarios met Class IA evidence, 9 case scenarios met Class IIB evidence, and for 5 case scenarios no guidelines were available (see Appendix II in the online-only Data Supplement).

For assessment of EVT decision-making, both during and outside regular working hours, we created time-specific case scenarios (daytime: 8:00 to 17:00 and nighttime: 22:00 to 7:00).

To evaluate the role of baseline brain imaging, participants were exposed to scenarios with good (ASPECTS [Alberta Stroke Program Early CT Score] of 8–10 or ischemic core <30 mL), moderate (ASPECTS of 5–7 or ischemic core 30 to 70 mL), and poor (ASPECTS of 0–4 or ischemic core >70 mL) baseline computed tomography imaging.[34,35] We categorized participants according to their expertise into neurologists (n=326), interventional radiologists (n=173), and others (n=108). The others category comprised 80 neurosurgeons, 5 internists, 2 geriatricians, and 21 participants with expertise on EVT decisions who did not disclose their expertise.

Outcome Measures

The primary outcome measure was the decision to use EVT. Participants were given multiple therapeutic choices for each case scenario (antiplatelet, anticoagulation, intravenous thrombolysis alone, EVT alone, combination therapies) to reflect current clinical practice. Secondary outcome measures included adherence to current EVT guidelines and gaps between current routine practice and ideal practice setting (no monetary or infrastructure restrictions).

Statistical Analysis

The primary analysis was based on multivariable logistic regression using a weight of evidence method that included all independent variables available from the survey. Independent variables were coded to the same scale for direct comparison of model parameters. The information value (IV) of independent variables, which represents the weight of each variable in relation to the outcome of interest, was reported. By convention, IV<0.02 indicates that the predictor is not useful; IV=0.02 to 0.1 means that the predictor has a weak relationship to the outcome; IV=0.1 to 0.3 suggests a relationship of medium strength; and IV≥0.3 represents a strong relationship with the outcome. The final multivariable logistic regression model reports variables with IV values ≥0.1. Standardized differences, which reflect the mean difference as a percentage of the SD of the mean, were used to evaluate clinical meaningfulness of statistically significant differences. Values >0.1 are considered clinically meaningful.[36] Mixed effects logistic regression modeling was applied for sensitivity analysis to ensure consistency with the weight of evidence approach. All tests were 2-tailed, and $P<0.05$ were considered significant.

Results

Of 1330 physicians invited to participate in UNMASK EVT, 835 (62.8%) initiated and 607 (45.6%) completed the study. Mean age was 44.8 (±8.6) years, and 97 (16.0%) were females. Most physicians (n=551; 90.8%) worked in academic institutions. The mean number of years in practice was 14.2 (±8.8), assessing on average 172 (±164) patients with stroke per year.

The Table summarizes baseline characteristics of the study population.

Factors Associated With Decision to Proceed With Endovascular Therapy

The most influential factors associated with EVT decision were baseline National Institutes of Health Stroke Scale and level of evidence (IV>30%), followed by baseline noncontrast computed tomography imaging (ASPECTS <4, 5–7, 8–10), age, yearly EVT cases per physician and center, aphasia/dysarthria, patients' living will and geographic region (IV=10%–29%; Figure 1A). Comorbidities, baseline functional status, anticoagulation therapy, physicians' demographics, and risk preferences had minimal influence on EVT decisions (IV=2%–9%; Figure 1B).

Mixed effects logistic regression with backward elimination revealed that age (per year increase in age OR, 0.99; 95% CI, 0.99–0.999; $P=0.017$), baseline stroke severity (National Institutes of Health Stroke Scale score of >15 versus National Institutes of Health Stroke Scale score of 0–5; OR, 3.6; 95% CI, 2.64–5.02; $P<0.001$) and ASPECTS (5–7 versus 0–4; OR, 7.28; 95% CI, 5.76–9.24; $P<0.001$) were the most relevant factors for EVT decision-making (see Table II in the online-only Data Supplement).

EVT Decisions by Level of Evidence and Specialty

Of 2208 responses for Class I evidence scenarios, 1917 (86.8%) agreed with pursuing EVT. Among the different specialists, neurologists had the lowest (84.8%) and interventional radiologists the highest values (89.3%; Figure 2A; $P=0.003$). Results were similar when combining Class I and IIB scenarios; 75.0% of 4690 responses favored EVT (72.3% neurologists versus 78.0% interventional radiologists versus 76.7% physicians of other specialists; $P=0.025$).

Table. Baseline Characteristics of Participants

Variable	Neurologists	Interventional Radiologists	Others
Number	326 (53.7)	173 (28.5)	108 (17.8)
Age, y; mean±SD	44.0±9.3	46.7±8.1	44.5±6.3
Female sex	74 (22.7)	9 (5.3)	14 (13.0)
Experience, y; mean±SD	14.1±9.2	13.9±7.6	14.8±9.3
Practice setting, academic	299 (91.8)	156 (90.2)	96 (89.0)
Number of patients with stroke whom participants cared for per y; mean±SD	258.3±164.9	49.3±48.3	107.6±117.7
Number of EVT patients whom participants cared for per y; mean±SD	32.0±32.2	49.9±45.9	36.2±31.7
Number of alteplase cases per center/y, mean±SD	122.0±113.5	176.8±165.9	118.8±160.5
Number of EVT cases per center/y, mean±SD	80.8±70.8	103.1±83.8	72.4±60.3
Region			
Australia/NZ	20 (6.1)	11 (6.4)	7 (6.5)
South Asia	23 (7.1)	10 (5.8)	8 (7.4)
East Asia	67 (20.6)	30 (17.3)	23 (21.3)
Europe	73 (22.4)	39 (22.5)	23 (21.3)
Near East	9 (2.7)	3 (1.7)	2 (1.8)
North America	115 (35.3)	65 (37.6)	38 (35.2)
South America	19 (5.8)	15 (8.7)	7 (6.5)

Numbers in brackets indicate percentages, unless otherwise specified. Alteplase indicates that intravenous thrombolysis was performed with alteplase. EVT indicates endovascular thrombectomy.

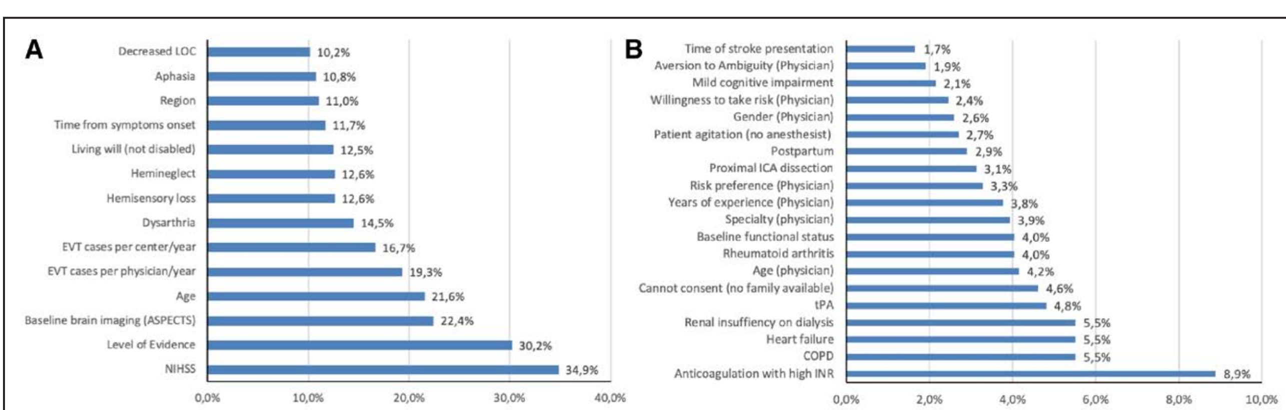

Figure 1. Factors associated with endovascular treatment (EVT) decisions. **A**, Represents moderate to strong factors associated with EVT decisions (information value [IV]≥10%). **B**, Represents factors with low association to EVT decisions (IV≤9). Numbers indicate the weight of each contributing factor in EVT decisions and expressed as percentage of the IV. ASPECTS indicates Alberta Stroke Program Early CT Score; COPD, chronic obstructive pulmonary disease; ICA, internal carotid artery; INR, international normalized ratio; LOC, level of conciousness; NIHSS, National Institutes of Health Stroke Scale; and tPA, tissue-type plasminogen activator.

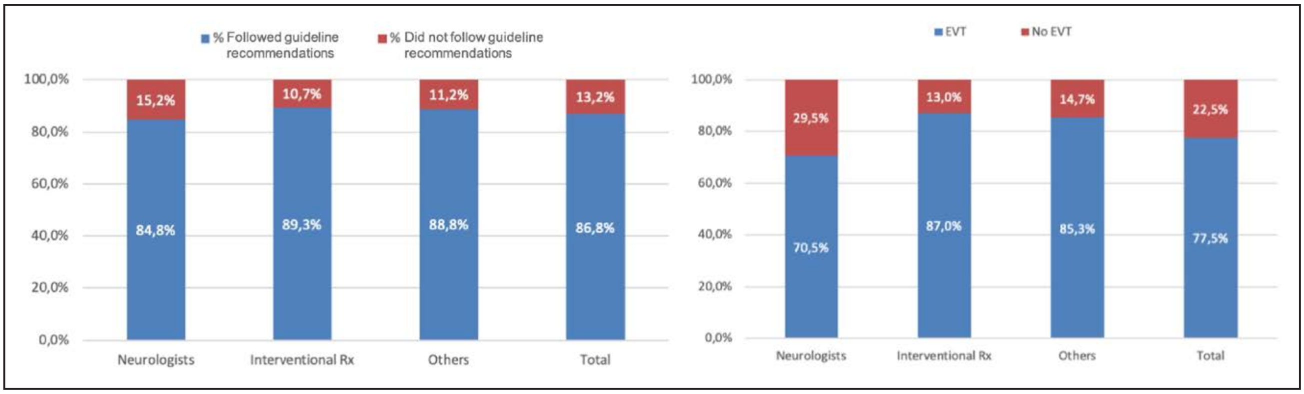

Figure 2. Endovascular treatment (EVT) decisions based on the level of evidence. **A**, Represents EVT decisions for case scenarios that met Class IA guidelines; χ^2 (2; N=2208)=11.93, *P*=0.003. **B**, Represents EVT decisions for case scenarios with no guidelines available; χ^2 (2; N=1380)=5.02, *P*=0.08. Rx indicates radiologists.

Of 1380 responses derived from case scenarios without guideline coverage, 1070 (77.5%) selected EVT. Overall, there were no differences in EVT decisions among specialties (Figure 2B; *P* for trend=0.08). However, there was a 16.5% difference in EVT decisions between neurologists and interventional radiologists (70.5% versus 87.0%; *P*<0.0001). There were no differences in EVT decisions by years of training (median split <13 years: 75.2% versus 75.8% for > 13 years; *P*=0.61) and no clinically meaningful significant differences in risk perception and tolerance to uncertainty among participants' specialties (see Table III in the online-only Data Supplement). The decision to pursue EVT varied among geographic regions; EVT rates for South East Asia (60.5%) and South America (58.5%) were lower than for Australia/New Zealand (80.8%), North East Asia (78.6%), Europe (79.5%), and North America (76.2%).

EVT Decisions by Baseline Brain Imaging and Time of the Clinical Assessment

Treatment differed significantly based on baseline imaging data (*P*<0.0001); for scenarios with ASPECTS ≥5 or ischemic core volume ≤70 mL, over 54% of responses favored combined therapy (intravenous alteplase plus EVT), whereas intravenous alteplase alone was chosen in only 12% and 18%, respectively (Figure 3). In cases with poor baseline imaging (ASPECTS ≤4 or ischemic core volume ≥70 mL), participants chose antiplatelet or anticoagulation therapy in 31%, alteplase alone in 11.9%, and EVT (alone or combined with alteplase) in 57.1% (Figure 3). Participants were more likely to give alteplase during nighttime and EVT alone during daytime (χ^2 for trend over 6070 responses; *P*=0.0002; Figure 4).

Clinical Gaps Between the Current and the Ideal Treatment Environment

The overall difference between the current working conditions and ideal practice setting was 15.5%. The most common shifts were from alteplase alone to alteplase plus EVT (n=257; 27.3%), from single therapy (alteplase or EVT alone) to combined alteplase plus EVT (n=172; 18.3%), from antiplatelet or anticoagulation to EVT alone (n=107; 11.4%), and from antiplatelet or anticoagulation to alteplase plus EVT (n=21; 2.2%).

Discussion

In this large multinational study, we evaluated 6070 therapeutic decisions from 607 stroke physicians from 38 countries. The most important factors associated with EVT decisions were the level of evidence, stroke severity (National Institutes of Health Stroke Scale), baseline brain imaging, patient age, clinical presentation, living will, participants' and centers' EVT experience and the geographic region. Interestingly, the presence of comorbidities, baseline functional status, physicians' demographics, or years of practice had minimal influence on EVT decisions. The vast majority (86.8%) of responses agreed with Class IA recommendations. Minor differences in the proportion

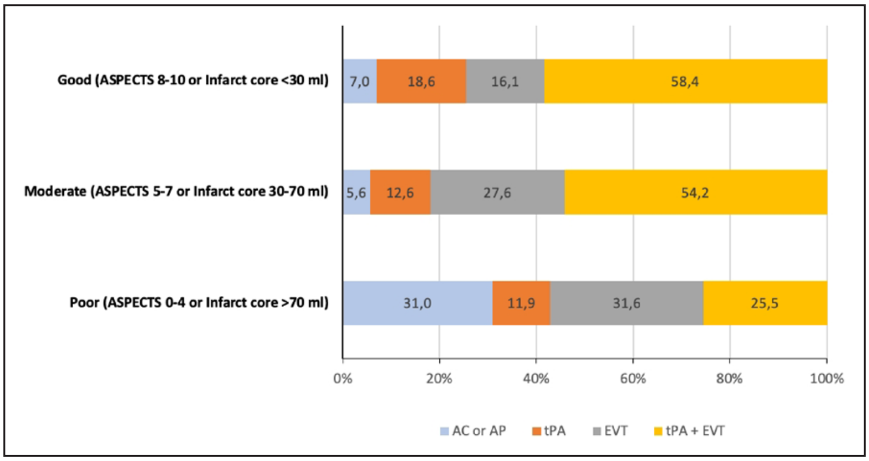

Figure 3. Descriptive analysis regarding therapeutic decisions based on baseline brain imaging information (ASPECTS [Alberta Stroke Program Early CT Score] and ischemic core volume). Values represent percentage of therapeutic decisions based on case scenarios with good, moderate, and poor brain imaging. AC or AP: anticoagulation or antiplatelet therapy, alteplase: intravenous thrombolysis. χ^2 for trend (N=6070 responses): *P*<0.0001. EVT indicates endovascular thrombectomy; and tPA, tissue-type plasminogen.

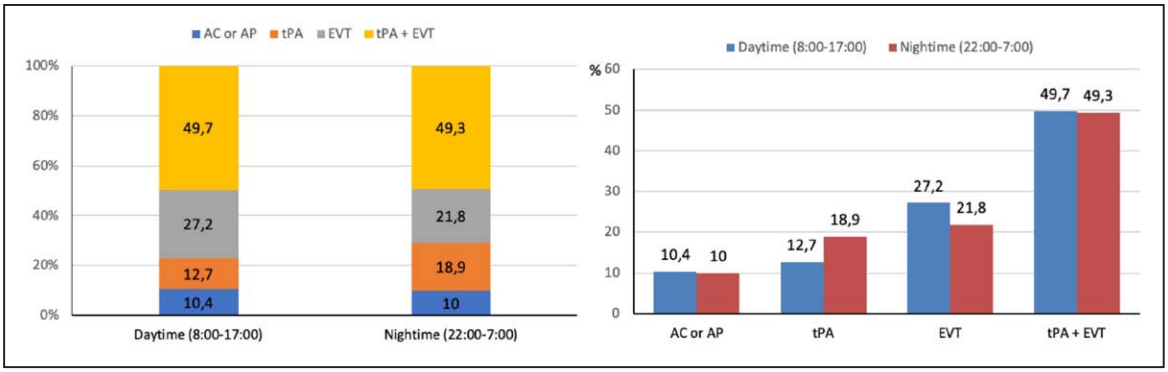

Figure 4. Descriptive analysis about therapeutic decisions based on time of the assessment. **A**, Illustrates therapeutic choices made at daytime and nighttime. **B**, Compares differences for each therapeutic choice by time of the day. The analysis of individual responses (n=6070) based on each assessed case scenario revealed that participants were more likely to give alteplase during nighttime and endovascular thrombectomy (EVT) alone during daytime (χ^2 for trend over 6070 responses; *P*=0.0002). No differences were noted between alteplase plus EVT between daytime and nighttime decisions. AC or AP: anticoagulation or antiplatelet therapy, alteplase: intravenous thrombolysis. tPA indicates tissue-type plasminogen.

of evidence-based responses among specialists were observed; neurologists had the lowest (84.8%) and interventional radiologists the highest (89.3%) tendency to favor EVT. Interestingly, most participants chose EVT even in scenarios without evidence for EVT (77.5% of 1380 responses). For example, it was surprising that 57.1% of participants elected for EVT for case scenarios with an ASPECT score lower than 4. However, the most likely explanation was the young age of patients in those case scenarios, suggesting that most participants heavily weighted the young age of the patient (and implicated higher chances of recovery) in EVT decisions even when brain imaging are discouraging. This decision represents an example of the last resource/opportunity thinking approach by attempting brain revascularization even when not indicated.

There was no association between therapeutic decision-making and participants' risk preferences and tolerance to uncertainty. More than half of the respondents chose EVT for cases with low ASPECTS (≤4) or high ischemic core volume (≥70 mL) that are usually associated with poor prognosis. We found a modest practice gap reflected by therapeutic switches between current and assumed ideal clinical settings in 15.5% of responses.

Our results help to improve our current understanding of therapeutic decision-making in acute stroke. Previous studies evaluating therapeutic decisions in outpatient settings for chronic conditions found an association between physicians' aversion to ambiguity/uncertainty and lack of treatment escalation.[33,37] Our study showed no association between ambiguity/uncertainty tolerance and treatment decisions for acute stroke care. This finding is reassuring; it seems that physicians are unlikely to be influenced by their personal risk preferences when prompt and accurate decisions are needed.

A low number of female physicians (15.9%) participated in the study, especially those trained in surgical specialties—this reflects the current stroke environment and also has been confirmed in previous studies.[38–40]

Our study has limitations that deserve comment. First, most participants were primarily practicing in academic centers, limiting generalizability of results to nonacademic centers. However, this reflects the fact that most endovascular stroke treatments are performed in academic centers. Further studies including nonacademic centers involved in acute stroke care are needed. Second, only few participants were female. Third, although we targeted a prespecified number of participants per country, our results concerning regional differences should be interpreted with caution. Fourth, the assessment of case scenarios may not fully capture decisions made in clinical practice, although specialists acknowledged that the scenarios reflect their daily practice well. Finally, evidence-based guidelines are constantly evolving and get updated when new data becomes available. It is possible that our results may change when new evidence becomes available (eg, nonguideline-based scenarios may become Class I evidence in the future).

Despite these limitations, our study is the first step in understanding the decision-making process and patient, physician, and healthcare level factors influencing EVT decisions. Using a novel approach that combines behavioral experiments and special analytical strategies applied to case-vignettes, UNMASK EVT helps unmask key determinants of EVT decisions in acute stroke care. Our results provide vital information to initiate discussions on how to overcome practice gaps in nonacademic settings, optimize transfer decisions, and implement educational strategies that ultimately lead to better outcomes and quality of life for patients with stroke.

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