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ABSTRACT

BACKGROUND AND PURPOSE: Results regarding the association of thrombus length, stent retriever length, and recanalization success in patients with acute ischemic stroke are inconsistent. We hypothesized that the ratio of thrombus length to stent retriever length may be of particular relevance.

MATERIALS AND METHODS: Patients with acute ischemic stroke undergoing stent retriever thrombectomy at our institution between January 2010 and December 2018 were reviewed retrospectively. Thrombus length was assessed by measuring the susceptibility vessel sign on SWI using a 1.5T or 3T MR imaging scanner. Multivariable logistic regression models were used to determine the association between thrombus length, stent retriever length, and thrombus length/stent retriever length ratio with first-pass recanalization, overall recanalization, and embolization in new territories. Results are shown as adjusted ORs with 95% CIs. Additional mediation analyses were performed to test for indirect effects on first-pass recanalization and overall recanalization success.

RESULTS: The main analysis included 418 patients (mean age, 74.9 years). Increasing stent retriever length was associated with first-pass recanalization. Decreasing thrombus length and lower thrombus length/stent retriever length ratios were associated with first-pass recanalization and overall recanalization. Thrombus length and stent retriever length showed no association with first-pass recanalization or overall recanalization once thrombus length/stent retriever length ratio was factored in, while thrombus length/stent retriever length ratio remained a significant factor in both models (adjusted OR, 0.316 [95% CI, 0.112–0.892]; $P = .030$ and adjusted OR, = 0.366 [95% CI, 0.194–0.689]; $P = .002$). Mediation analyses showed that decreasing thrombus length and increasing stent retriever length had a significant indirect effect on first-pass recanalization mediated through thrombus length/stent retriever length ratio. The only parameter associated with embolization in new territories was an increasing thrombus length/stent retriever length ratio (adjusted OR, 5.079 [95% CI, 1.332–19.362]; $P = .017$).

CONCLUSIONS: Information about thrombus and stent length is more valuable when combined. High thrombus length/stent retriever length ratios, which may raise the risk of unsuccessful recanalization and embolization in new territories, should be avoided by adapting stent retriever selection to thrombus length whenever possible.

ABBREVIATIONS: aOR = adjusted OR; ENT = embolization into unaffected (new) territories; eTICI = expanded TICI; FP = first-pass; FPR = first-pass recanalization; SL = stent retriever length; SVS = susceptibility vessel sign; TL = thrombus length

Increasing thrombus size has a negative impact on the efficacy of intravenous thrombolysis in patients with acute ischemic stroke.[1] It is uncertain whether this also holds true for recanalization after mechanical thrombectomy. Whereas some studies have found no association,[2-4] others suggest that the likelihood of successful recanalization after mechanical thrombectomy also decreases with increasing thrombus size.[5-8] Opinions are also divided on whether stent retriever size plays a role in this context.[9-11] We hypothesized that recanalization success is predominantly influenced by the thrombus-to-stent retriever length ratio (TL/SL), which ultimately affects clinical outcome. Therefore, our goal was to evaluate the direct and indirect influence of thrombus length (TL), stent retriever length (SL), and TL/SL on first-pass recanalization (FPR),

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overall recanalization, and the risk of embolization in previously unaffected (new) territories (ENT).

MATERIALS AND METHODS

Inclusion Criteria

We conducted a retrospective post hoc analysis of patients with acute ischemic stroke who presented to Bern University Hospital for mechanical thrombectomy. The clinical and radiologic data presented in this study were gathered by manual review of patients with acute ischemic stroke who underwent mechanical thrombectomy at our hospital between January 2010 and December 2018. The inclusion criteria were as follows: 1) a final clinical diagnosis of acute ischemic stroke; 2) admission MR imaging with SWI available; 3) susceptibility vessel sign (SVS) apparent on SWI; 4) occlusion of at least one intracranial artery on angiography; and 5) the patient having undergone stent retriever thrombectomy. SWI quality was classified as "poor" if the SVS was not assessable due to major artifacts. If the thrombus was masked because of its proximity to the skull base or overlaid by other pathologies (eg, hemorrhage), SVS was considered "technically undeterminable." Patients with poor-quality SWI or technically undeterminable SVS status were excluded.

Most patients with stroke admitted to our institution are primarily scanned using MR imaging. However, the final decision on whether to perform MR imaging or CT is made by the neuroradiologists and neurologists in charge on a case-by-case basis depending on clinical aspects and contraindications. This study was approved by the local ethics committee (Bernese/Swiss Stroke Registry: Kantonale Ethikkommission für die Forschung Bern, Bern, Switzerland, amendment access number: 231/2014 and BEYOND-SWIFT registry, access number: 2018–00766). Patients gave written or oral consent for the use of their data for research. Before January 1, 2015, the need for consent was waived in accordance with regulations of the Swiss law and the local ethics committee.

Data Collection

We collected information on demographics, baseline characteristics, and clinical data, such as age, sex, history of stroke, medication before acute ischemic stroke (antiplatelet therapy, anticoagulants, statins), and documented cardiovascular risk factors such as hypertension, diabetes mellitus, dyslipidemia, and smoking habits. Furthermore, we recorded the following admission data: systolic and diastolic blood pressure, glucose levels, NIHSS score, and stroke subtypes according to Trial of Org 10172 in acute stroke treatment (TOAST) classification. Moreover, IV thrombolysis before imaging (transfer patients) and before mechanical thrombectomy as well as time from symptom onset/last seen well to admission and to mechanical thrombectomy and time from groin puncture to recanalization were documented.

Technical Information: MR Imaging

Imaging was performed on a 1.5T or 3T MR imaging unit (1.5T: Magnetom Avanto or Magnetom Aera; 3T: Magnetom Verio; Siemens). SWI using the 1.5T scanners was performed with the following parameters: TR, 49 ms; TE, 40 ms; flip angle, 15.0°; section thickness, 1.6, 1.8, or 2.0 mm; and intersection gap, 0 mm. 3T SWI was performed with the following parameters: TR, 27 ms; TE, 20 ms; flip angle, 15.0°; section thickness, 2.0 mm; and intersection gap, 0 mm.

Imaging Analysis

Naggara et al[12] have shown excellent correlation between TL as measured on T2* gradient-echo sequences and those determined by DSA. However, SWI has proved to be superior to T2* gradient-echo sequences for evaluating the SVS.[13] The presence and length of the SVS were evaluated retrospectively by 1 independent neuroradiologist (N.F.B.) with 5 years of experience who was blinded to all outcome parameters and had no role in patient treatment. SWI was classified as SVS+ if a distinct signal loss corresponding to an acutely occluded, symptomatic intracranial artery could be identified regardless of how its diameter compared with that of the contralateral artery. TL was measured in a multiplanar SWI reconstruction along the axis of the occluded vessel and recorded in millimeters (Figs 1 and 2). If the SVS was discontinuous (ie, a fractured or heterogeneous clot), the visible sections of the thrombus demonstrating a circumscribed signal loss on SWI were measured and the total was calculated. MR imaging field strength and time from symptom onset to imaging were documented for each case. Additionally, the DWI-ASPECTS was evaluated.

DSA and Stent Retriever Thrombectomy

The primary site of occlusion was determined on the basis of conventional angiography findings. Tandem occlusions were also documented. Stent retriever thrombectomy was performed by experienced interventional neuroradiologists according to the current clinical practice guidelines and institutional protocols. The ex vivo length of the first-line stent retriever device as provided by the manufacturer as well as the total number of passes performed during mechanical thrombectomy were recorded. The expanded TICI (eTICI) score[14] was documented after the first pass and at the end of mechanical thrombectomy. Successful FPR and overall recanalization were defined as an eTICI of 2b or better. DSA was screened for ENT and for peri-interventional complications (vasospasm, dissection, and perforation) by a research fellow with 3 years of experience (J.K.). SL was used to calculate the TL/SL. In addition, all patients were categorized binarily as TL>SL if TL was longer than SL and TL≤SL if TL was not longer than SL. The first-line endovascular treatment technique was categorized as follows: 1) stent retriever alone, 2) stent retriever with a balloon-guided catheter, 3) stent retriever with contact aspiration, or 4) stent retriever with both contact aspiration and a balloon-guided catheter.

Outcome

The NIHSS was evaluated by a neuroradiologist 24 hours after treatment. Mortality and favorable outcome 90 days after treatment were assessed according to the mRS during clinical follow-up by a neurologist or a study nurse. Patients were considered functionally independent if the mRS was ≤2 90 days after treatment. Symptomatic intracranial hemorrhage within 48 hours after stent retriever thrombectomy was assessed according to the European Cooperative Acute Stroke Study (ECASS II).[15]

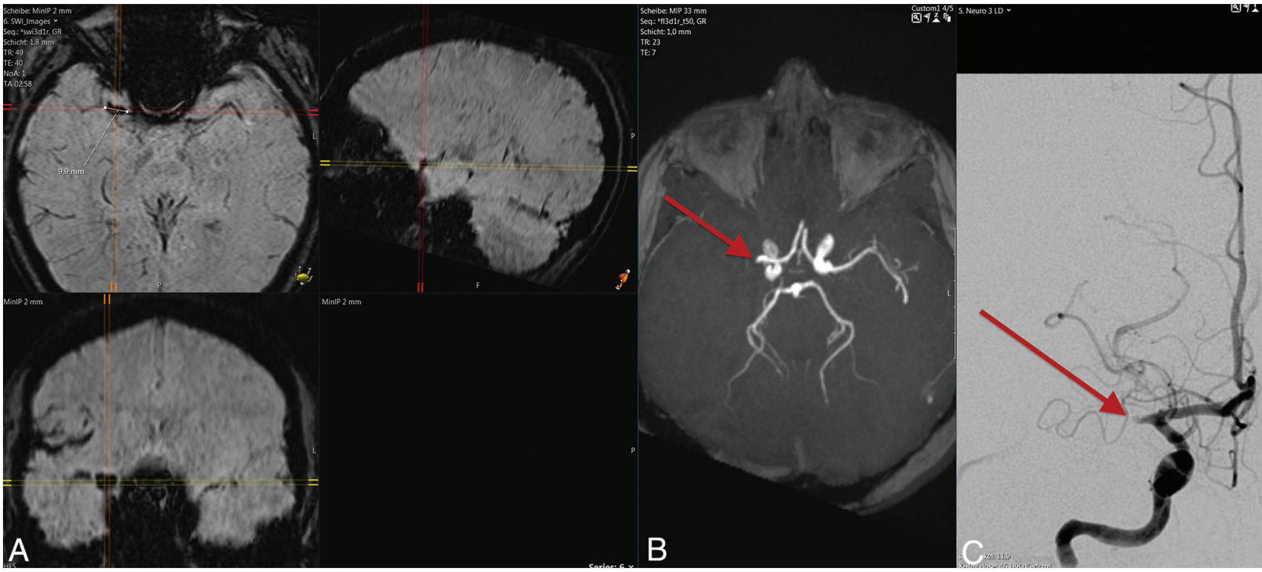

FIG 1. A male patient with acute ischemic stroke after occlusion of the right MCA main trunk (M1-segment). The occlusive thrombus can be seen on SWI (*A*) as a circumscribed loss of signal along the main trunk of the MCA. Corresponding images of the arterial TOF sequence (*B*) and DSA (*C*) show the same vessel occlusion. Thrombus measurement was performed on multiplanar SWI reconstruction along the longitudinal axis of the occluded vessel (*C*). The *red arrow* points to the proximal end of the vessel occlusion on arterial TOF and DSA.

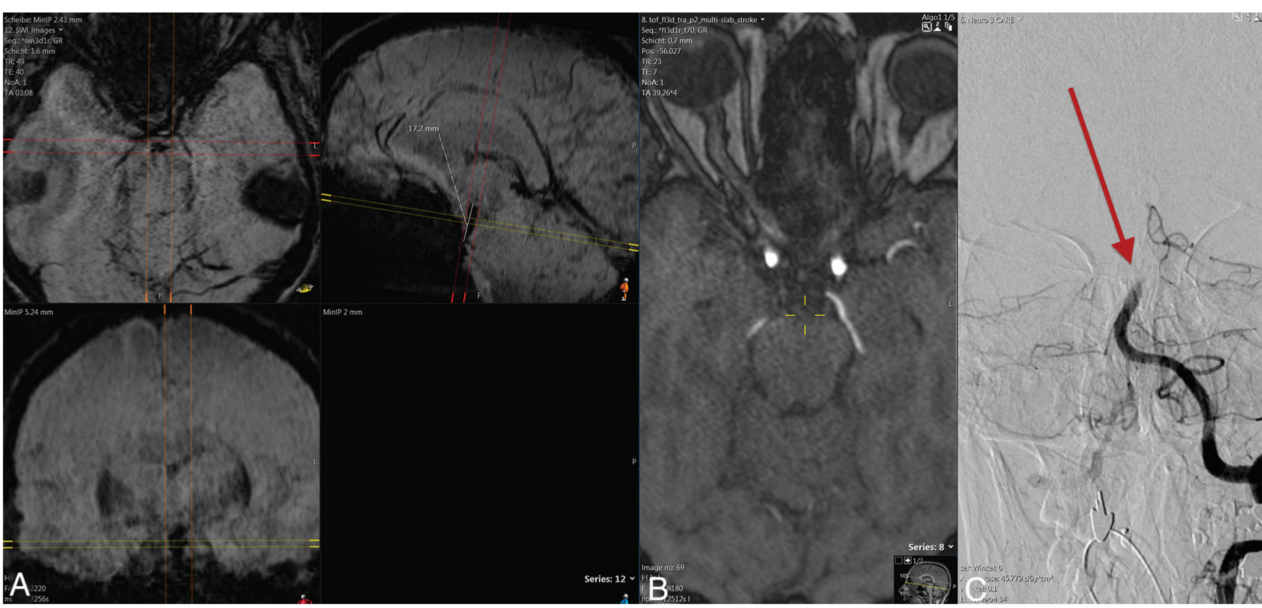

FIG 2. A patient with acute ischemic stroke after occlusion of the basilar artery. The occlusive thrombus can be seen on SWI (*A*) as a circumscribed loss of signal along the basilar artery. Corresponding images of the arterial TOF sequence (*B*) and DSA (*C*) show the same vessel occlusion. The *yellow crosshairs* are centered on the middle portion of the vessel occlusion on arterial TOF (*B*). Thrombus measurement was performed on multiplanar SWI reconstruction along the longitudinal axis of the occluded vessel (*C*). The *red arrow* points to the proximal end of the vessel occlusion on digital subtraction angiography.

Statistical Analysis

Data were analyzed using SPSS Statistics software (Version 25.0; IBM). Continuous variables were compared using the Mann-Whitney *U* test; and categoric variables, with the χ^2 test. Multivariable binary logistic regression analyses were performed to determine the association between TL, SL, and TL/SL with FPR, overall recanalization, and ENT. Adjustment was made for all cofactors with $P < .150$ as well as additional cofactors that are known or suspected to influence the variables of interest (ie, age, sex, bridging therapy, stroke subtype, symptomatic intracerebral hemorrhage). Mediation analyses were performed to test the indirect effects of TL and SL on FPR and overall recanalization after adjusting for age, sex, previous stroke, primary site of occlusion, stroke subtype, tandem occlusion, bridging thrombolysis, and first-line endovascular treatment technique. Results with 2-tailed *P* values $<$ .05 were considered statistically significant and are shown as median (interquartile range, 25%–75%), median comparisons with respective P values, or adjusted OR (aOR) with 95% CIs.

RESULTS

Between January 2010 and December 2018, at Bern University Hospital, 1317 patients underwent endovascular treatment for acute ischemic stroke; 676 underwent MR imaging on admission. SWI was performed in 624 of those cases. A further 168 patients were excluded due either to poor-quality SWI, technically undeterminable SVS status, or absence of SVS. A stent retriever device was used 422 times alone or in combination with another device or devices among the remaining cases as part of the first-line retrieval technique; stent size was documented in 418 of them. The Online Supplemental Data outline the patient-selection process. On average, TL was 14 mm (10–20 mm), while SL was 20 mm (20–30 mm). In 11 patients, TL was >40 mm and hence exceeded the longest stents available. Online Supplemental Tables 1 and 2 show all the results for first-pass (FP) recanalizers versus non-FP recanalizers. The Online Supplemental Data list all stent retriever devices used in this study.

Association between Thrombus-to-Stent Size Ratio and First-Pass Recanalization

TL was significantly longer for non-FP recanalizers than for FP recanalizers (15 versus 13 mm, $P = .013$), whereas SL was significantly shorter for non-FP recanalizers than for FP recanalizers (20 versus 20 mm, $P = .003$). TL exceeded the length of the chosen stent more frequently in non-FP recanalizers than in FP recanalizers (TL>SL: 20.2% [$n = 33/163$] versus 12.0% [$n = 31/259$], $P = .018$). TL/SL was greater for non-FP recanalizers than for FP recanalizers (0.71 versus 0.55, $P = .000$). A subgroup analysis showed a first-pass recanalization rate of 36.4% ($n = 4/11$) when TL exceeded the longest stents available (>40 mm), which was significantly lower than the overall FPR rate of 61.4% ($n = 259/422$). In 3 separate multivariate binary regression models, decreasing TL and TL/SL (TL: aOR, 0.955 [95% CI, 0.930–0.981]; $P = .001$; TL/SL: aOR, 0.296 [95% CI, 0.162–0.543]; $P = .000$), as well as increasing SL (aOR, 1.046 [95% CI, 1.016–1.077]; $P = .002$) were associated with FPR after adjusting for all cofactors with $P < .15$ (Online Supplemental Table 1) as well as for age, sex, previous stroke, stroke subtype, bridging therapy, primary site of occlusion, tandem occlusion, and first-line endovascular treatment technique. TL and SL showed no significant association with FPR once the TL/SL was factored in (TL: aOR, 0.996 [95% CI, 0.950–1.045], $P = .885$; SL: aOR, 1.029 [95% CI, 0.998–1.061], $P = .070$), whereas decreasing TL/SL remained significantly associated with FPR (TL/SL after including TL: aOR, 0.316 [95% CI, 0.112–0.892], $P = .030$; TL/SL after including SL: aOR, 0.366 [95% CI, 0.194–0.689]; $P = .002$). The distribution of first-pass eTICI according to TL/SL quartiles is visualized in Fig 3.

The Online Supplemental Data illustrate the adjusted probabilities of achieving FPR depending on the TL/SL. A sensitivity analysis with FPR defined as TICI 3 on first pass did not change this observation (Online Supplemental Data). A subgroup analysis exclusively examining mechanical thrombectomies performed with Solitaire (Medtronic) stents of 4-mm diameter (Online Supplemental Data) confirmed that these findings were independent of stent diameter or stent design.

On mediation analysis, decreasing TL showed no direct effect on FPR (aOR, −0.006 [95% CI, −0.046 to 0.035]; $P = .784$), but a significant and positive indirect effect on FPR mediated through TL/SL was observed (effect, 0.046 [95% bootstrap CI, 0.011–0.096]; $P < .05$). In another mediation analysis, increasing SL showed no direct effect on FPR (aOR, 0.026 [95% CI, −0.002 to 0.083]; $P = .073$), but it had a significant and positive indirect effect on FPR mediated through SL/TL (effect, 0.018 [95% bootstrap CI, 0.004–0.037]; $P < .05$). Further subgroup analyses examining the impact of favorable-versus-unfavorable TL/SL on FPR can be found in the Online Supplemental Data. TL and SL are not significantly different between FP recanalizers and non-FP recanalizers if categorized by the TL/SL quartile (Online Supplemental Data). As illustrated by the Online Supplemental Data, there are no significant differences between TL quartile distribution in FP recanalizers and non-FP recanalizers if categorized according to TL/SL quartiles.

Association between Thrombus-to-Stent Size Ratio and Overall Recanalization

TL was also longer for overall nonrecanalizers than for overall recanalizers (16 versus 13 mm, $P = .025$). SL was significantly shorter for nonrecanalizers than for recanalizers (20 versus 20 mm, $P = .007$). TL exceeded the length of the chosen stent more frequently in overall nonrecanalizers than in overall recanalizers (29.0% [$n = 20/69$] versus 12.8% [$n = 49/382$], $P = .001$). TL/SL was significantly greater for overall nonrecanalizers than for overall recanalizers (0.75 versus 0.6, $P = .000$). After adjusting for the effects of all parameters with $P < .15$ when comparing overall recanalizers with overall nonrecanalizers (Online Supplemental Table 1) as well as age, sex, stroke subtype, previous stroke, and tandem occlusion, SL showed no significant association with overall recanalization (aOR, 1.029 [95% CI, 0.989–1.071]; $P = .157$). In 2 separate multivariable regression models using the same covariates, decreasing TL and TL/SL were associated with overall recanalization (TL: aOR, 0.950 [95% CI, 0.919–0.982], $P = .003$; TL/SL: aOR, 0.272 [95% CI, 0.130–0.570], $P = .001$). In another multivariate regression model using the same covariates and including both TL and TL/SL, TL showed no association with overall recanalization (aOR, 1.016 [95% CI, 0.944–1.093]; $P = .670$), whereas a decreasing TL/SL remained significantly associated with overall recanalization (aOR, 0.206 [95% CI, 0.047–0.907]; $P = .037$). On mediation analysis, a decreasing TL showed no direct effect on overall recanalization (aOR, −0.053 [95% CI, −0.119 to 0.014]; $P = .119$) but proved to have a significant and positive indirect effect on overall recanalization mediated through the TL/SL (effect, 0.101 [95% bootstrap CI, 0.046–0.212]; $P < .05$).

Association between Thrombus-to-Stent Size Ratio and ENT

TL and SL were not significantly different between patients who showed ENT on angiography and those who did not (TL: 21 versus 14, $P = .120$; SL: 20 versus 20, $P = .245$). TL exceeded the

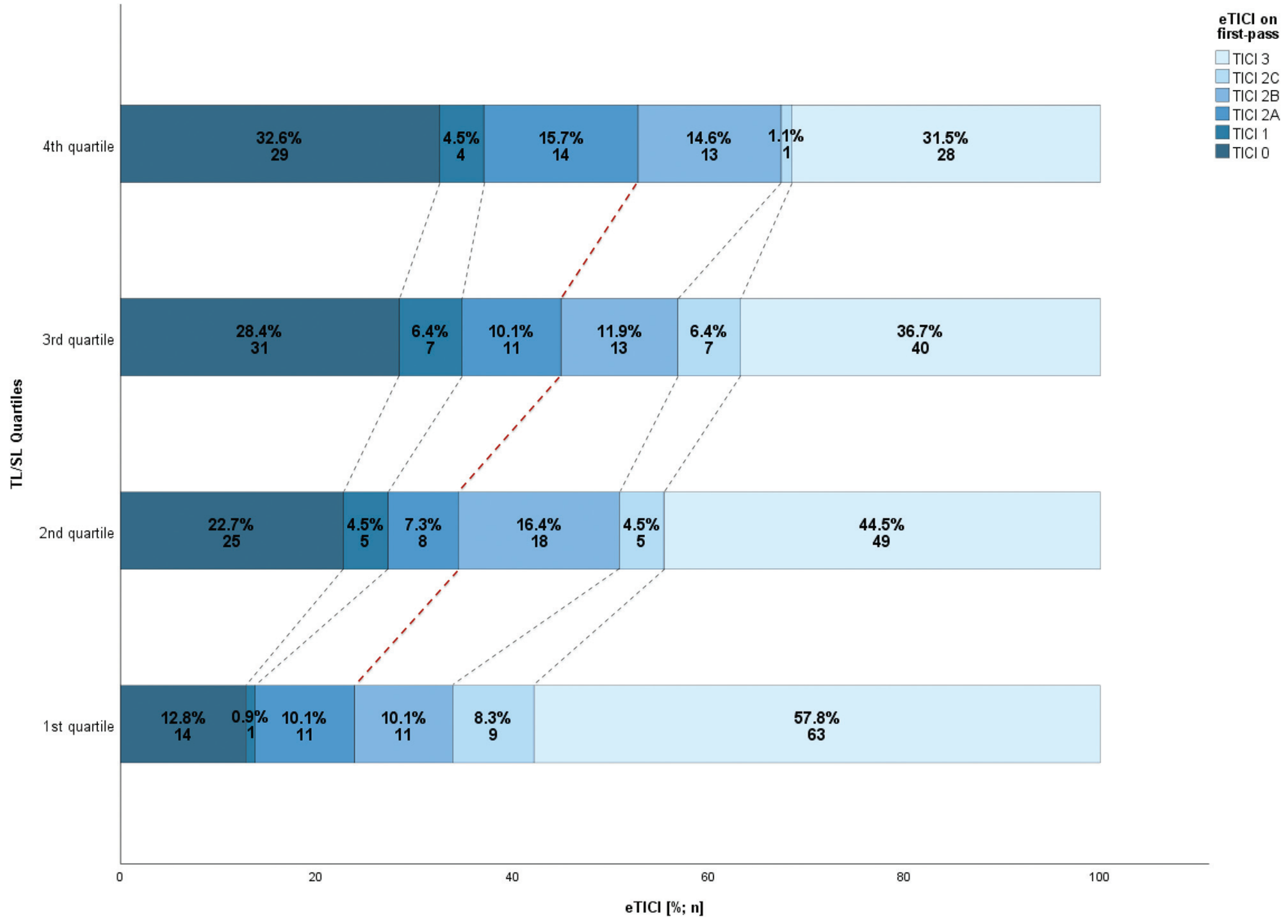

FIG 3. First-pass eTICI distribution according to TL/SL quartiles ($P = .004$). The quartile limits are as follows: 0.25-quartile = 0.425; 0.5-quartile = 0.600; 0.75-quartile = 0.900. The *black and red dotted lines* mark the eTICI margins. The *red dotted line* also marks the threshold for successful recanalization defined as eTICI ≥ 2B.

length of the chosen stent more frequently in patients in whom ENT was observed later (36.8% [$n = 7/19$] versus 14.4% [$n = 62/431$], $P = .005$). The TL/SL ratio was significantly higher for patients who showed ENT (0.79 versus 0.60, $P = .037$). After adjusting for all cofactors with $P < .15$ when comparing patients with and without ENT (Online Supplemental Data) as well as age, sex, previous stroke, stroke subtype, and first-line endovascular treatment technique, an increasing TL/SL ratio was associated with ENT (aOR, 5.079 [95% CI, 1.332–19.362]; $P = .017$).

DISCUSSION

The main findings of this study are as follows: Increasing SL was associated with FPR. Decreasing TL and TL/SL were associated with FPR and overall recanalization. TL and SL alone showed no association with FPR or overall recanalization once TL/SL was factored in, whereas TL/SL remained a significant factor in both models. Mediation analyses showed that a decreasing TL had a significant and positive indirect effect on FPR and overall recanalization mediated through TL/SL, whereas SL had a significant and positive indirect effect on FPR success mediated through SL/TL. Increasing TL/SL was the only parameter associated with ENT.

Previous studies have come to different conclusions about the influence of thrombus and stent size on recanalization success.[2-11] Multiple explanations for these discrepancies are possible: 1) Different parameters have been used to evaluate thrombus size (thrombus length,[5,8] thrombus volume,[6] clot burden score[7]). 2) Sensitivity may differ depending on the imaging tool or technique used (MR imaging [2,5,7] versus CT [6] versus DSA;[2] T2* gradient recalled-echo[5,7] versus SWI;[2] and field strength and manufacturer of the MR imaging scanner). 3) If thrombus size is evaluated by measuring the SVS, differences in the SVS definition may influence patient selection and thrombus-size measurement.[2,4] 4) Fractured clots may hinder uniform and reproducible thrombus measurement. 5) Comparability of studies that examine TL is often limited owing to differing inclusion criteria (ie, M1 or anterior acute ischemic stroke only[2,7,9-11] versus other occlusion patterns[5]). 6) Because many institutions have a preferred set of retrieval devices, stent size comparison is usually limited to 1–3 size categories.[9-11] 7) Stent retriever thrombectomy may be performed in combination with a balloon-guided catheter[16] and/or contact aspiration.[17] The first-line endovascular treatment technique that may influence recanalization success has not always been documented.[10] 8) High-volume centers may achieve recanalization more often and with fewer attempts in difficult cases than low- or medium-volume centers, thus limiting the comparability of results from different centers. 9) Thrombus and stent size as individual parameters may not affect recanalization success directly but rather have an indirect influence, which is mediated by their relation to each other.

Our results support the assumption that the last of these explanations is likely to account for most of the discrepancies so far. Because the physical interaction between retriever device and clot is at the center of successful stent retriever thrombectomy, we hypothesized that looking at thrombus size in relation to stent size may provide more specific information than is gained by considering them separately. This hypothesis is based on the supposition that the chances of clot-to-device interaction are not necessarily higher for longer stents if the occlusive clot is small enough. On the other hand, we expected that large thrombi would not inevitably lead to an increased risk of fragmentation or distal migration if the size of the stent retrieval device selected is adequate. Our analyses show that TL and SL are both associated with recanalization success but suggest that the TL/SL ratio serves as a more informative variable. Using mediation analyses, we were able to demonstrate that decreasing TL and increasing SL had a significant and positive indirect influence on successful FPR mediated through TL/SL or SL/TL, respectively, whereas decreasing TL also had a positive indirect influence on overall recanalization mediated through TL/SL.

Our results also show that FPR, which was more often achieved by avoiding a high TL/SL, led to more favorable clinical outcomes 90 days after treatment in first-pass recanalizers.

Data regarding the influence of thrombus or stent size on the risk of embolization in previously unaffected territories are scarce. Seker et al[3] found no association between TL and ENT, which was supported by our results. However, the TL/SL was associated with ENT, confirming the additional value of this parameter. To improve comparability, we adjusted all our statistical analyses for the primary site of occlusion, which may affect interventional and clinical outcome parameters.[18] The use of balloon-guided catheters has been found to increase recanalization success[16] and reduce the risk of ENT.[19] Therefore, we also took the first-line endovascular treatment technique into account in our calculations.

Our results suggest that avoiding a high TL/SL by adjusting stent retriever selection according to the presumed TL on admission imaging may be beneficial. If such an assessment is not feasible, the neurointerventionalist should reduce the probability and risks of a high TL/SL by selecting the longest stent retriever device with which she or he is comfortable from those that are otherwise adequate. Although stent retrievers with shorter diameters are believed to pose less risk for vascular injury,[20] some studies have shown that longer stents might be just as safe.[11,21] Future studies may examine whether this assumption would remain true for new stent retriever devices, which could be even longer than the ones currently available. Nonetheless, we can assume that the application of unnecessarily long stents carries the risk of peri-interventional complications, especially if the diameter of the occluded vessel is small and the neurointerventionalist is unaccustomed to the specific stent retriever device used. Devices designed to have an adequate length but little radial force might be an option, particularly when operating in distal vessel segments.[22] The preinterventional assessment of TL could lower this risk by allowing a more nuanced stent retriever selection. In this context, possible shortening of the stent retriever device depending on the deployment technique should be considered beforehand. Regardless of the stent size and brand, extra caution is necessary when working with new or unaccustomed devices.

Limitations

This was a retrospective single-center study, which may limit generalizability. Patients who were ineligible for MR imaging or showed complete recanalization on DSA before stent retriever thrombectomy were excluded, possibly leading to selection bias. A previous study has shown that baseline criteria and reperfusion outcome of patients with stroke may differ depending on the initial imaging technique.[23] TL was measured assuming that all thrombus margins are delineated by the SVS. Although some studies have shown that the SVS allows accurate TL measurement,[2,12] TL assessment was not double-checked via DSA in this study, possibly leading to some over- or underestimation of TL due to blooming artifacts and/or fibrin-rich segments in heterogeneous thrombi. TL may have been underestimated in intracranial ICA occlusions that extended extracranially through the skull base. In a small number of patients, TL may have changed between admission MR imaging and mechanical thrombectomy due to thrombosis, thrombolysis, or fragmentation.

Clot density, which may impact recanalization success, could not be assessed on MR imaging. Clot composition, which may also influence recanalization success, was not evaluated in detail. Stent selection was at the discretion of the neurointerventionalist, allowing possible selection bias. Because some thrombi exceeded the longest stents available, it is uncertain whether longer stents would have been equally safe and efficient in those cases.

Ex vivo SL as provided by the manufacturer was considered for analysis. Although stent retriever devices are not designed to change in length after deployment, in vivo SL might differ slightly depending on deployment technique and vascular anatomy. Finally, data on first-pass eTICI may not always reflect the true success of the intervention in patients with multiple vessel occlusions within the same territory.

CONCLUSIONS

Thrombus length and stent length provide more useful information when considered in relation to one another. A high TL/SL ratio, which may raise the risk of unsuccessful recanalization and ENT, should be avoided whenever possible. The preinterventional assessment of TL allows a more nuanced stent retriever selection and may, thereby, help to avoid unnecessarily long stents, which would increase the risk of peri-interventional complications.

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