

Patient profiles contribute to differences in quality metrics of stroke centers

Matthias Ungerer, MD, Nima Haji Begli, MD, Miriam Heyse, MD, Jan Purrucker, MD, Jens Regula, MD, Anne Berberich, MD, Ludovico Ciolli, MD, Simon Nagel, MD, Peter Ringleb, MD, Christoph Gumbinger, MD.

ABSTRACT

الأهداف: فحص هذه العلاقة من خلال مقارنة الملفات الشخصية للمرضى في مستشفيات مرتبطين بشكل وثيق وفحص ارتباطهم بمقاييس الجودة.

المنهجية: أجرينا دراسة جماعية بأثر رجعي تقارن بين مراكز السكتة الدماغية الشاملة (CSC) بمستشفى جامعي ووحدة السكتة الدماغية المحلية (LSU) باستخدام بيانات ضمان الجودة التي جمعت بشكل روتيني على مدار عامين. كان كلا المستشفيات منتسبين بشكل وثيق، وتقاسموا موارد مهمة، وتم تناوب الطاقم الطبي بين المستشفيات. قارنا ملفات تعريف المرضى بالإضافة إلى مقاييس الجودة المعترف بها دوليًا وفحصنا ارتباط الملفات الشخصية بمقاييس الجودة.

النتائج: علاجنا 2,462 مريضًا في CSC و 726 في LSU. كان وقت الدخول إلى وقت التصوير ووقت الدخول إلى وقت الإبرة أطول في LSU. كان معدل انحلال الجلطات الجهازية أقل في LSU. اختلفت ملفات تعريف المرضى بشكل كبير وارتبطت بأوقات مختلفة من وقت الدخول إلى وقت التصوير ومن وقت الدخول إلى وقت الإبرة وكذلك معدلات انحلال الخثرة الوريدية، حتى عند تعديلها لمستوى خدمة السكتة الدماغية. كانت الإجراءات التشخيصية للسكتة الدماغية متشابهة. اختلفت إدارة خروج المرضى بشدة.

الخلاصة: على الرغم من أن LSUs و CSCs هم مقدمو الرعاية الأولية في مناطقهم، إلا أن الاختلافات في ملفات تعريف المرضى قد تساهم في الاختلافات في معايير الأداء. قد يؤدي تعديل ملفات تعريف المرضى إلى تحسين إمكانية مقارنة جودة رعاية السكتة الدماغية التي تقدمها المستشفيات التي تنتمي إلى مستويات مختلفة لخدمة السكتة الدماغية.

Objectives: To examine this association by comparing patient profiles in 2 closely affiliated hospitals and by examining their association with quality metrics.

Methods: We performed a retrospective cohort study comparing a university level comprehensive stroke centers (CSC) with its teaching hospital and local

stroke unit (LSU) using routinely collected quality assurance data over a 2 year period. Both hospitals were closely affiliated, shared important resources and medical staff rotated amongst both hospitals. We compared patient profiles as well as internationally recognized quality metrics and examined the association of profiles with quality metrics.

Results: A total of 2,462 patients were treated in the CSC and 726 in the LSU. The LSU had a longer door-to-image and door-to-needle times. Rate of systemic thrombolysis was lower in the LSU. Patient profiles differed significantly and were associated with door-to-image and door-to-needle times as well as intravenous thrombolysis rates, even when adjusted for stroke service level. The diagnostic procedures for stroke work-up were similar. Discharge management differed strongly.

Conclusion: Although LSUs and CSCs are the primary care providers in their respective regions, differences in patient profiles may contribute to differences in performance parameters. Adjusting for patient profiles may improve the comparability of the quality of stroke care provided by hospitals belonging to different stroke service levels.

*Neurosciences 2020; Vol. 25 (4): 292-300
doi: 10.17712/nsj.2020.4.20190100*

From the Department of Neurology (Ungerer, Begli, Heyse, Purrucker, Regula, Berberich, Nagel, Ringleb, Gumbinger), University Hospital Heidelberg, Heidelberg; from the Department of Neurology (Purrucker, Regula), GRN-Klinik Sinsheim, Sinsheim, Germany; and from the Stroke Unit, Neurology Unit, Department of Neuroscience (Ciolli), Ospedale Civile, Azienda Ospedaliera Universitaria di Modena, Modena, Italy.

Received 29th October 2019. Accepted 7th May 2020.

Address correspondence and reprint request to: Dr. Christoph Gumbinger, Department of Neurology, University Hospital Heidelberg, Heidelberg, Germany. E-mail: christoph.gumbinger@med.uni-heidelberg.de

Stroke remains a devastating disease causing severe disability and high mortality rates despite novel treatments and overall declining death rates in developed countries.¹ Improvement of treatment standards through optimization and standardization of treatment is an essential tool to further decrease death rates and improve outcomes. Concepts to reduce both prehospital and in-house delays to increase intravenous thrombolysis (IVT) rates have been explored extensively in recent years and continue to be refined.²⁻⁴

The introduction of specialized stroke units contributed significantly to better outcomes and lower mortality for stroke patients by setting requirements for training of staff, patient monitoring, diagnostic work-up and by improving discharge practices.⁵⁻⁷ In addition to setting internationally recognized standards for treatment of stroke patients, standardization of treatment and introduction of comparable quality metrics allowed for both routine data collection and benchmarking of hospitals, admission wards and treatment regimes. This can be used to further improve care and outcomes. However, differences in quality metrics remain significant between primary stroke care providers despite standardization of care. This is in part attributable to differences in in-house standards and local treatment practices. Large-scale studies have suggested that quality metrics such as rates of IVT and endovascular treatments are higher in comprehensive stroke centers (CSC) than primary care centers (LSU) and risk-adjusted mortality rates can be different as well.⁸ Other studies comparing CSCs and LSUs have confirmed that clinical outcomes are dependent on the level of stroke care.⁹ Most studies have suggested that individual hospital profiles have a significant impact on patient outcomes, mostly attributed to availability of stroke units and patient volumes.¹⁰ However, these studies considered hospitals that function mostly independently and with significant disparities in training of medical staff which may affect quality of treatment while little is known about the causes for differences in quality metrics seen among closely affiliated hospitals that share similar resources and operating procedures. We believe that patient profiles may affect quality metrics such as door-to-needle and door-to-image times significantly and relevant differences in patient profiles

may contribute to differences in other quality metrics for stroke care in otherwise similar hospitals.

We explored differences in-between a major urban university hospital, which is a CSC, and its closely affiliated rural teaching hospital with its LSU both in terms of patient profiles and quality metrics. We hypothesized that, although both hospitals are primary stroke care providers for their respective regions and both share a similar basic clinical infrastructure and rotating medical staff, patient profiles contribute to differences in quality metrics of stroke care.

Methods. A retrospective cohort study comparing a university hospital and CSC with its closely affiliated teaching hospital which is in itself a LSU was performed. Both hospitals belong to the same stroke network, are located in close proximity (40 km) to one another and provide similar standards of stroke unit care with 24/7 access to CT angiography. Medical staff (both residents and attending physicians) rotate in-between both hospitals and therefore receive similar training and have a similar level of expertise. Close cooperation between the 2 hospitals includes both teleneurology and teleradiology services during nights and on weekends. The CSC covers all aspects of acute stroke care including a subspecialized emergency room (ER) for neurological patients and 24/7 endovascular therapy. All other forms of treatment and diagnostic workups are also provided in the teaching hospital. The ER in the teaching hospital is staffed by a consultant neurologist during office hours and by internal medicine residents at night and on weekends with teleneurology services being provided by trained staff at the CSC. Only patients requiring endovascular interventions were transferred to the CSC.

Data was collected as part of a prospective stroke registry of stroke patients treated as in-house patients in the federal state Baden-Wuerttemberg of Germany. Patients were recruited consecutively over a 2 year period. All hospitals must supply quality metrics data to this registry for patients aged ≥ 18 years admitted within 7 days of symptom onset with the diagnosis of stroke (10th revision of the International Classification of Diseases) as outlined in the German Social Code V, 112, so patient consent to data collection is not necessary (collected data is anonymized). Participating hospitals receive annual quality reports, which incorporate a benchmarking of the hospital regarding quality metrics. Plausibility checks of data are carried out regularly by local authorities and accuracy of raw data is examined in random samples. If the data reported by a hospital does not meet the strict quality criteria measures such as financial penalties may be introduced to improve

Disclosure. Authors have no conflict of interests, and the work was not supported or funded by any drug company.

documentation and transmission rates.¹¹ Details on data collection and quality can be found elsewhere.¹¹

Standardized documentation for the stroke registry was filled out by treating physicians and nursing staff. Data collected included demographic parameters; past medical history; mode of hospital admission; time of hospital admission; admission ward (intensive care unit, stroke unit, normal ward); admission to a neurology or internal medicine department; timing and type of diagnostic procedures; rtPA treatment rates and door-to-needle time; treatment complications; discharge information; and intra-hospital mortality. The pre-stroke modified Rankin Scale (pmRS) score was estimated at admission. Only patients eligible for IVT were included in comparisons of IVT rates and door-to-needle times. We classified ICD-10 codes I61 and I62 as intracranial hemorrhage and I63 as ischemic stroke. Severity of stroke was assessed with the National Institutes of Health Stroke Scale (NIHSS).¹² Information on comorbidities was also collected. We were not able to collect follow up information as this was not intended as part of the stroke registry and data privacy laws in Germany prohibit collection of follow-up data without patient consent. The analysis was approved by the Medical Faculty Heidelberg, University of Heidelberg (S339-2012). This study was conducted according to the principles of the Helsinki declaration.

Part of the source data is automatically transferred from the electronic medical records or is documented manually in the electronic patient management system. Source files were filled out by the treating physicians. Incoming data were checked based on plausibility checks, raw data are checked by random sampling. A structured dialogue, an instrument of quality improvement, is initiated if a hospital shows abnormal quality aspects namely, rate of data transmission or consistency of data.

Statistical analysis. Data are presented as means and standard deviations (SD), as relative frequencies in the form of percentages or median with interquartile range in the text. Relative frequencies were always described as values of the CSC versus LSU in the text. For the statistical analysis, Fisher's exact test and Chi-squared tests were used to determine differences of frequencies and the t-test and Mann-Whitney-U-Test were used to determine differences of means and medians. P-values <0.05 were considered to show a significant difference. Association of patient profiles with quality metrics was calculated using binary regression analysis expressed as adjusted odds ratios for stroke service level of the admitting hospital. Unadjusted regression analysis

demonstrating association of the hospital of admission with quality metrics was included for comparison.

Results. We analyzed data from 2 annual quality assurance reports over 2 years, one from a university hospital with a CSC and one from a community hospital with an LSU.

Patient profiles and mode of admission. Altogether, 2,462 patients from the CSC and 726 patients from the LSU fulfilled the inclusion criteria for acute stroke treatment. The proportion of patients with intracerebral hemorrhage (ICH) was higher in the CSC (18% versus 4%), while higher proportions of patients with cerebral ischemia (66% versus 73%) and transient ischemic attack (TIA; 17% versus 23%) were treated in the LSU. Mean age was significantly lower in the CSC (68.6 years [14.2] versus 73.8 years [12.1]). Patients in the CSC were more frequently male than in the LSU (57% versus 49%). A higher proportion of patients with low stroke severity, measured as NIHSS score of 0, were found in the LSU (14% versus 25%). Self-referral was more frequent in the LSU (15% versus 24%), while a higher proportion of patients admitted to the CSC came via emergency physicians and emergency medical services (43% versus 32%). Referral from other hospitals occurred more often in the CSC than in the LSU. Comorbidities, such as prior stroke, arterial hypertension, atrial fibrillation, diabetes mellitus, and hypercholesterolemia were more frequent in the LSU. Patients had a lower pre-stroke Rankin Scale in the CSC (Table 1).

Performance in quality parameters regarding acute stroke management. The proportion of patients receiving acute stroke treatment (namely, IVT) is a quality parameter of stroke care. It is defined as the proportion of all patients between 18-80 years receiving IVT. This was over 4 times higher in the CSC than in the LSU (17% versus 4%; Table 2). The quality parameter of door-to-needle-time is defined as the proportion of patients having a door-to-needle-time of less than one hour. Fewer patients were treated with a short door-to-needle-time in the LSU (≤ 60 min: 69% [CSC] versus 29% [LSU]). The time to initial imaging (door-to-image-time) is regarded as part of the door-to-needle-time and is also a quality parameter of stroke care. Again, door-to-image times were shorter in the CSC (within 30 min of admission: 38% versus 22%).

Regression analysis showed that, in addition to stroke service level, patient profiles such as stroke severity assessed by NIHSS, state of consciousness, aphasia at admission and duration of symptoms were associated with door-to-needle-times, door-to-image-

Table 1 - Characteristics of the study population.

Characteristics	CSC (n=2,462)	LSU (n=726)	P-value
Female sex, n (%)	1,051 (42.7)	367 (50.6)	<0.001
Age in years, mean (SD)	68.62±14.21	73.82±12.14	<0.001
<i>Stroke type, n (%)</i>			<0.001
TIA	408 (16.6)	168 (23.1)	
Intracranial hemorrhage	436 (17.7)	28 (3.8)	
Ischemia	1,618 (65.7)	530 (7.3)	
<i>Comorbidities, n (%)</i>			
Prior stroke	625 (25.4)	194 (26.7)	0.469
Arterial hypertension	1,930 (78.4)	641 (88.3)	<0.001
Diabetes mellitus	593 (24.1)	200 (27.5)	0.063
Atrial fibrillation	534 (21.7)	211 (29.1)	<0.001
Hypercholesterolemia	820 (33.3)	517 (71.2)	<0.001
pmRS, median (IQR)	0 (0-2)	1 (0-2)	<0.001
<i>pmRS, n (%)</i>			<0.001
0	1435 (58.3)	333 (46.9)	
1	398 (16.2)	162 (22.3)	
2	323 (13.1)	100 (13.8)	
3	213 (8.7)	83 (11.4)	
4	84 (3.4)	39 (5.5)	
5	9 (0.4)	9 (1.2)	
<i>Referral to hospital, n (%)</i>			<0.001
Self	370 (15.0)	171 (23.6)	
Emergency services	1049 (42.6)	232 (32.0)	
Other hospital	627 (25.5)	124 (17.2)	
Primary care physician	346 (14.1)	179 (24.7)	
In-house stroke	70 (2.8)	19 (2.6)	

CSC - comprehensive stroke centers, LSU - local stroke unit, IQR - interquartile range, pmRS - pre-stroke modified rankin scale, mRS - modified rankin score; PCP - primary care physician, TIA - transient ischemic attack

times and IVT rates (Table 4). We found a number of factors such as age, pmRS, NIHSS, duration of symptoms and specific clinical symptoms at admission that were strongly associated with door-to-image times. Atrial fibrillation was associated significantly with both door-to-image time and increased the odds significantly for treatment with IVT. Previous stroke significantly decreased the odds for being treated with IVT. All other comorbidities were not associated with quality metrics.

Performance in quality parameters of stroke work-up. Details of stroke etiology work-up and intrahospital stroke care are summarized in Table 3. The proportion of patients that received neurosonography (extra- and intracranial) were comparable in the 2 hospitals, although symptomatic carotid stenosis was found more often in the CSC (10% versus 6%).

Transthoracic- or transesophageal-echocardiography was performed slightly more often in the LSU (77% versus 87%). The LSU had slightly higher rates of early secondary stroke prevention with platelet inhibitors (66% for the CSC versus 75% for the LSU), platelet inhibitors at discharge (59% CSC versus 68% LSU), and oral anticoagulation (23% CSC versus 28% LSU). Prophylaxis of thrombosis was more often initiated at the CSC (95% versus 77%), but more CSC patients suffered from complications such as pneumonia and thrombosis (15% versus 8%). Symptomatic intracerebral hemorrhage as a complication of thrombolytic therapy occurred to about the same extent in both hospitals.

Discharge management. Information about discharge are summarized in Table 3. A higher

Table 2 - Acute prehospital and early intrahospital stroke care.

Characteristics	CSC (n=2,462)	LSU (n=726)	P-value
mRS at admission, median (IQR)	3 (2-5)	2 (1-4)	<0.001
<i>mRS at admission</i>			<0.001
0	226 (9.2)	90 (12.4)	
1	250 (10.2)	127 (17.5)	
2	405 (16.5)	170 (23.4)	
3	518 (21.0)	152 (20.9)	
4	445 (18.1)	117 (16.1)	
5	618 (25.1)	70 (9.6)	
NIHSS, mean (SD)	7.69 ± 8.98	4.01 ± 5.56	<0.001
<i>NIHSS on admission*</i>			<0.001
4-25	1,139 (48.5)	242 (33.9)	
1-3 or >25	856 (36.4)	295 (41.4)	
0	354 (15.1)	176 (24.7)	
<i>Admission ward</i>			<0.001
Normal ward	146 (5.9)	17 (2.3)	
Stroke Unit	1,832 (74.4)	693 (95.5)	
ICU	484 (19.7)	16 (2.2)	
<i>Door-to-image-time</i>			<0.001
≤30 min	736 (37.5)	120 (22.3)	
>30 min	1,227 (62.5)	417 (77.7)	
Image before admission	385 (15.6)	160 (22.0)	
<i>Modality of first image</i>			0.058
CT	2,002 (81.3)	612 (84.3)	
MRI	430 (17.5)	111 (15.3)	
None/not documented	30 (1.2)	3 (0.4)	
<i>Intravenous thrombolysis</i>			<0.001
None	2031 (82.9)	693 (95.9)	
After admission	367 (15.0)	30 (4.1)	
Before admission	53 (2.2)	0 (0)	
<i>Door-to-needle time</i>			<0.001
≤60min	287 (68.7)	9 (29.0)	
>60 min	131 (31.3)	22 (71.0)	
Symptomatic ICH	36 (8.1)	2 (6.5)	0.537

Values are presented as number and percentage (%).
 CSC - comprehensive stroke centers, LSU - local stroke unit
 mRS - modified Rankin Score; NIHSS - National Institute for Health Stroke Scale; ICU - intensive care unit, i.v. - intravenous;
 iICH - intracranial hemorrhage. Some of the values may not add up to the total number of patients included due to missing values* (namely, for patients with in-house stroke no "door"-time could be calculated)

Table 3 - Intra-hospital stroke care, diagnostics and discharge.

Characteristics	CSC (n=2462)	LSU (n=726)	P-value
TTE/TEE	1,888 (76.7)	631 (86.9)	<0.001
<i>Neurosonography</i>			
IC	2,257 (91.7)	655 (90.2)	0.230
EC	2,227 (90.5)	678 (93.4)	0.014
Symptomatic ICA stenosis	252 (10.2)	42 (5.8)	<0.001
Thrombosis prophylaxis	2,328 (95.0)	558 (77.2)	<0.001
PFI <48 hour	1,611 (65.7)	539 (74.6)	<0.001
PFI at discharge	1,446 (59.0)	493 (68.2)	<0.001
(Planned) anticoagulant	573 (23.4)	205 (28.4)	0.007
<i>Complications</i>			
All complications	375 (15.3)	59 (8.2)	<0.001
Pneumonia	120 (4.9)	25 (3.4)	0.10
Thrombosis/pulmonary embolism	5 (0.0)	1 (0.0)	0.99
Others	283 (11.5)	40 (5.5)	<0.01
<i>Discharge modality</i>			<0.001
Home	1,208 (49.0)	490 (67.5)	
Rehabilitation	269 (10.9)	136 (18.7)	
Other hospital	781 (31.7)	48 (6.6)	
Nursing home	1 (0.0)	23 (3.2)	
Other	203 (8.2)	29 (4.0)	
Intrahospital mortality	202 (8.2)	26 (3.6)	<0.001
Mean length of stay (days), mean ± SD	6.19 ± 7.24	7.06 ± 5.03	0.002

Values are presented by number and percentage (%).

CSC - comprehensive stroke centers, LSU - local stroke unit, TTE/TEE - transthoracic or transesophageal echocardiogram, IC - intracranial, EC - extracranial, ICA - internal carotid artery, PFI - platelet function inhibitor

proportion of patients in the CSC were transferred to other hospitals (32% versus 7%). The LSU had higher rates of regular discharge home (49% versus 68%). The quality parameter of direct discharge to rehabilitation (11% to 19%) was achieved in a higher proportion of patients in the LSU. Discharge to a nursing home was more frequent in the LSU (0% versus 3%). Mean length of hospital stay were lower in the CSC (mean 6.2 days in the CSC versus 7.1 days in the LSU).

Discussion. Our main findings were as follows: between the 2 hospitals we found 1) differences in patient profiles, especially in baseline characteristics, stroke symptoms and severity at admission; 2) relevant differences in quality metrics for acute stroke care (namely, door-to-needle-time and door-to-image-time); 3) evidence that patient profiles affect results of quality metrics; 4) comparable coverages of stroke

Table 4 - Association of patient characteristics and stroke service level with quality metrics (binary regression analysis, adjusted for stroke service level).

Characteristics	P-value	Odds ratio	Lower CI	Upper CI
Intravenous thrombolysis rate after admission to the emergency room (yes versus no)				
<i>Baseline characteristics</i>				
Age	<0.001	1.020	1.011	1.028
Gender	0.100	1.196	0.966	1.482
pmRS	0.516	1.029	0.943	1.124
Admission type	<0.001	0.735	0.658	0.823
<i>Symptoms/severity of stroke at admission</i>				
NIHSS	<0.001	1.044	1.033	1.055
Consciousness*	0.014	0.743	0.586	0.943
Paresis	<0.001	1.583	1.397	1.694
Aphasia	<0.001	1.418	1.199	1.677
Dysarthria	<0.001	1.840	1.559	2.172
Duration of symptoms (<1h; 1-24h; >24h)	<0.001	2.856	2.141	3.810
Hospital (LSU versus CSC)†	<0.001	0.240	0.163	0.351
Door-to-image-time >30 minutes				
<i>Baseline characteristics</i>				
Age	<0.001	0.988	0.982	0.995
Gender	0.833	0.982	0.830	1.162
pmRS	0.002	0.899	0.841	0.961
Admission type	<0.001	1.182	1.090	1.283
<i>Symptoms/severity of stroke at admission</i>				
NIHSS	<0.001	0.944	0.934	0.954
Consciousness*	<0.001	0.745	0.630	0.879
Paresis	<0.001	0.654	0.603	0.709
Aphasia	<0.001	0.668	0.578	0.772
Dysarthria	<0.001	0.520	0.452	0.598
Duration of symptoms (<1h; 1-24h; >24h)	<0.001	0.687	0.602	0.783
Hospital (LSU versus CSC)†	<0.001	2.084	1.668	2.604
Door-to-needle-time >1 hour				
<i>Baseline characteristics</i>				
Age	0.666	0.997	0.983	1.011
Gender	0.921	1.021	0.684	1.523
pmRS	0.141	1.136	0.958	1.347
Admission type	0.157	1.222	0.926	1.612
<i>Symptoms/severity of stroke at admission</i>				
NIHSS	<0.001	1.050	1.023	1.077
Consciousness*	<0.001	2.349	1.552	3.557
Paresis	0.220	1.154	0.918	1.452
Aphasia	<0.001	1.927	1.348	2.754
Dysarthria	0.221	1.264	0.868	1.842
Duration of symptoms (<1h; 1-24h; >24h)	0.043	0.534	0.290	0.981
Hospital (LSU versus (SC)†	<0.001	5.355	2.400	11.950
CSC - comprehensive stroke centers, LSU - local stroke unit, pmRS - prestroke modified Rankin Scale, NIHSS - National Institute of Health Stroke Scale				
*awake, drowsie, comatose; †unadjusted, included for comparison				

work-up in both hospitals, but differences in discharge management.

Our results suggested that patient profiles at the CSC and LSU differed significantly. Patients admitted to the rural LSU were older with higher pmRS and lower stroke severity as assessed by NIHSS score at admission. Rural communities in developed countries have been found to have a different age distribution, higher frequency of comorbidities and less effective risk factor control.¹³ It has been described that these factors, together with inferior access to centers offering high quality stroke care, could contribute to worse clinical outcomes in rural communities. Rural communities in the United States have therefore been described as an “underserved minority” in terms of stroke care and more comprehensive stroke networks have been established to increase coverage in these areas.¹³ Geographical distance to the next hospital is unlikely to have had a significant impact in our study, since both hospitals are located in relatively close proximity (within 40 km) with comparable size of catchment areas and similar basic infrastructure. Despite both hospitals being primary care providers in their regions, patients with more severe strokes were presented to the CSC explaining in part why stroke severity and IVT rates were greater in the CSC. This is likely to affect both quality metrics and patient outcomes and translates to higher complication rates in the CSC where more severely affected patients were treated.

We also found relevant differences in the quality metrics for acute stroke care. In particular the proportion of patients receiving IVT was 4 times higher in the CSC. This is in line with other analyses of IVT rates in relation to stroke service level,^{8,14} although it has been shown that a stroke network (consisting of LSUs) can achieve IVT rates similar to those of a CSC.¹⁵ Age and preexisting disabilities are known predictors of thrombolytic therapy, and both differed significantly between the LSU and CSC and can in part explain the differences in quality metrics found in-between both hospitals.¹⁶ The quality parameter of door-to-needle-time showed a higher proportion of patients with a door-to-needle-times of ≤ 1 hour in the CSC. A subgroup of patients (namely, those on oral anticoagulation) require specialized diagnostic procedures (namely, bedside coagulation testing), which is not available in the LSU and could account for some of the difference.¹⁷ In addition to other patient related factors (namely, history of hypertension, previous stroke, stroke severity), the main predictor of door-to-needle-time discussed in current literature is patient volume,¹⁸ which was smaller in the LSU. Similarly, door-to-image-times of >30 minutes were much more frequent in the LSU when

compared to the CSC. However, stroke service level of the admitting hospital did not fully explain the observed differences in quality metrics observed in this study and it has been shown that similar door-to-needle-times are achievable in a stroke network, even if they include smaller stroke centers.¹⁶ Since both hospitals shared a number of important resources, in particular trained medical staff which rotated in-between hospitals and is an important contributor to quality of treatment, substantial differences in patient profiles or differences in in-house standards must therefore explain the difference. Although some of this difference can be explained by the fact that the CSC provides a specialized neurological emergency room, we believe that this does not fully explain the difference. We therefore performed a statistical analysis of our data to identify associations of patient profiles with quality metrics while adjusting for hospital of admission. We were able to demonstrate in this analysis that several patient characteristics were independently associated with quality metrics. This included patient age, pmRS, NIHSS at presentation, clinical symptoms at presentation, type of admission as well as stroke service level. Previous stroke and atrial fibrillation were also associated with IVT rates. Other comorbidities were not associated with quality metrics.

The subacute management and stroke work-up were similar in the CSC and the LSU (for example, rate of ultrasound examination of the vessels supplying the brain of echocardiography). As stroke work-up follows standardized diagnostic procedures, independent of patient profiles, the completeness of stroke-work up was comparable between the stroke service levels, suggesting that differences in the stroke-work up could be used as a parameter of quality of care. Also, there was a comparable rate of neurosonology. Overall, we found good evidence that the establishment of stroke units contributes to similar standards of care for hospitalized stroke patients in the CSC and LSU. In the CSC, more patients presented with symptomatic carotid stenosis (10% versus 6%), which may be attributable to the lower mean age.¹⁹ The higher rate of complications in the CSC (15% versus 8%) and the lower rate of patients on antithrombotic therapy or anticoagulation may be influenced by patient profiles, especially greater stroke severity and given the higher proportion of patients treated in an intensive care unit. The rate of hemorrhagic effacement after IVT was similar in both hospitals (8% versus 6% in LSU), representing similar confidence in the quality of IVT. The mean length of stay was longer in the LSU than in the CSC, possibly resulting from the higher rate of patients transferred to other hospitals from the CSC. More patients were directly transferred from the LSU to a rehabilitation facility or were

discharged home. As a result of different transfer and discharge practices, the value of using the length of stay as a quality parameter to compare hospitals is reduced.

Importance of findings. We were able to show that baseline patient characteristics as well as other aspects of patient profiles can affect quality metrics significantly, even when adjusted for stroke service level. This is important, since adjustment for these factors in future studies could enhance the comparability of hospitals and quality metrics in future studies and in clinical routine. We were also able to demonstrate that, although the LSU and CSC in this study are closely affiliated, have a distance of only 40 km, and share important resources, relevant differences in both patient profiles and quality metrics can persist. Adjustment of the suggested factors and possibly for stroke service level should therefore be strongly considered in future studies. Future studies should also examine the reasons for differences in quality metrics and patient outcomes in-between stroke service levels further in an effort to optimize patient treatment in hospitals providing lower service levels in underserved communities.

Study limitations. We only compared a single LSU with a single CSC, and this limits the generalizability of the results, but our analysis aimed to show that (unadjusted) benchmarking in some quality metrics could be influenced by differences in patient profiles and we did not intend to estimate the magnitude of this effect. Stroke patients referred to other hospitals were not included. We could not investigate a possible impact of the exact distance to the treating hospital on quality metrics since we did not have this information. Not all parameters were documented for all patients (missing data) namely, for patients who had imaging before admission no admission-to-image-time could be calculated. We only compared the performance in selected quality metrics, which also limits the generalizability of the results. We performed a mostly descriptive data analysis with no means of stratifying for diverse markers such as age, comorbidities, or pre-stroke mRS. Although both the LSU and CSC share important resources such as medical staff, basic organization of stroke treatment and teleneurological and teleneuroradiological services during nights and on weekends, differences in logistics, in particular in the organization of emergency room care, do remain. We therefore adjusted all calculated odds ratios for stroke service level of the hospital of admission to account for this effect.

In conclusion, the direct comparison of relevant quality metrics of acute stroke care is limited by differences in patient profiles between CSCs and LSUs.

A possible way to reduce bias in benchmarking of different hospitals would be to adjust for differences in patient profiles and to perform the benchmarking according to the stroke service level. The reasons for the lower overall performance in acute stroke management in the LSU should be further explored.

Acknowledgment. We would like to thank Scribendi (www.scribendi.com) for English language editing.

References

1. Yang Q, Tong X, Schieb L, Vaughan A, Gillespie C, Wiltz JL, et al. Vital signs: Recent trends in stroke death rates - United States, 2000-2015. *Morb Mortal Wkly Rep* 2017; 66: 933-939.
2. Kobayashi A, Czlonkowska A, Ford GA, Fonseca AC, Luijckx GJ, Korv J, et al. European Academy of Neurology and European Stroke Organization consensus statement and practical guidance for pre-hospital management of stroke. *Eur J Neurol* 2018; 25: 425-433.
3. Wang H, Thevathasan A, Dowling R, Bush S, Mitchell P, Yan B. Streamlining workflow for endovascular mechanical thrombectomy: Lessons Learned from a Comprehensive Stroke Center. *J Stroke Cerebrovasc Dis* 2017; 26: 1655-1662.
4. Ragoschke-Schumm A, Walter S, Haass A, Balucani C, Lesmeister M, Nasreldein A, et al. Translation of the "time is brain" concept into clinical practice: Focus on prehospital stroke management. *Int J Stroke* 2014; 9: 333-340.
5. Stroke Unit Trialists' Collaboration. Organised inpatient (stroke unit) care for stroke (Review) Organised inpatient (stroke unit) care for stroke. *Cochrane Database Syst Rev* 2013;11: CD000197.
6. Indredavik B, Bakke F, Solberg R, Rokseth R, Haaheim LL, Holme I. Benefit of a stroke unit: a randomized controlled trial. *Stroke* 1991; 22: 1026-1031.
7. Jorgensen HS, Kammersgaard LP, Nakayama H, Raaschou HO, Larsen K, Hubbe P, et al. Treatment and rehabilitation on a stroke unit improves 5-year survival. A community-based study. *Stroke* 1999; 30: 930-933.
8. Man S, Zhao X, Uchino K, Hussain MS, Smith EE, Bhatt DL, et al. Comparison of Acute Ischemic Stroke Care and Outcomes between Comprehensive Stroke Centers and Primary Stroke Centers in the United States. *Circ Cardiovasc Qual Outcomes* 2018; 11: e004512.
9. Meretoja A, Roine RO, Kaste M, Linna M, Roine S, Juntunen M, et al. Effectiveness of primary and comprehensive stroke centers: PERFECT stroke: A nationwide observational study from Finland. *Stroke* 2010; 41: 1102-1107.
10. Park HK, Kim SE, Cho YJ, Kim JY, Oh H, Kim BJ, et al. Quality of acute stroke care in Korea (2008-2014): Retrospective analysis of the nationwide and nonselective data for quality of acute stroke care. *Eur Stroke J* 2019; 4: 337-346.
11. Gumbinger C, Reuter B, Wiethölter H, Bruder I, Rode S, Drewitz E, et al. A consecutive and prospective stroke database covers the state of Baden-Wuerttemberg with 10.8 million inhabitants in Germany. *Neuroepidemiology* 2013; 41: 161-168.
12. Rost NS, Bottle A, Lee JM, Randall M, Middleton S, Shaw L, et al. Stroke severity is a crucial predictor of outcome: An international prospective validation study. *J Am Heart Assoc* 2016; 5: pii: e002433.

13. Leira EC, Phipps MS, Jasne AS, Kleindorfer DO. Time to treat stroke patients in rural locations as an underserved minority. *Neurology* 2017; 88: 422-423.
14. Moradiya Y, Crystal H, Valsamis H, Levine SR. Thrombolytic utilization for ischemic stroke in US hospitals with neurology residency program. *Neurology* 2013; 81: 1986-1995.
15. Gumbinger C, Reuter B, Hacke W, Sauer T, Bruder I, Diehm C, et al. Restriction of therapy mainly explains lower thrombolysis rates in reduced stroke service levels. *Neurology* 2016; 86: 1975-1983.
16. Hubert GJ, Meretoja A, Audebert HJ, Tatlisumak T, Zeman F, Boy S, et al. Stroke Thrombolysis in a Centralized and a Decentralized System (Helsinki and Telemedical Project for Integrative Stroke Care Network). *Stroke* 2016; 47: 2999-3004.
17. Rizos T, Horstmann S, Jenetzky E, Spindler M, Gumbinger C, Möhlenbruch M, et al. Oral anticoagulants - A frequent challenge for the emergency management of acute ischemic stroke. *Cerebrovasc Dis* 2012; 34: 411-418.
18. Groot AE, van Schaik IN, Visser MC, Nederkoorn PJ, Limburg M, Aramideh M, et al. Association between i.v. thrombolysis volume and door-to-needle times in acute ischemic stroke. *J Neurol* 2016; 263: 807-813.
19. Boehme AK, Siegler JE, Mullen MT, Albright KC, Lyster MJ, Monlezun DJ, et al. Racial and gender differences in stroke severity, outcomes, and treatment in patients with acute ischemic stroke. *J Stroke Cerebrovasc Dis* 2014; 23: e255-e261.

References

- * References should be primary source and numbered in the order in which they appear in the text. At the end of the article the full list of references should follow the Vancouver style.
- * Unpublished data and personal communications should be cited only in the text, not as a formal reference.
- * The author is responsible for the accuracy and completeness of references and for their correct textual citation.
- * When a citation is referred to in the text by name, the accompanying reference must be from the original source.
- * Upon acceptance of a paper all authors must be able to provide the full paper for each reference cited upon request at any time up to publication.
- * Only 1-2 up to date references should be used for each particular point in the text.

Sample references are available from:
http://www.nlm.nih.gov/bsd/uniform_requirements.html