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Quantifying neurological function in patients undergoing transcatheter aortic valve implantation

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ABSTRACT

Background: Transcatheter aortic valve implantation (TAVI) is a routine procedure that is often performed on older adults that are high-risk patients with severe aortic stenosis. Patients after TAVI may experience neurological complications. However, there is a lack of objective neurological testing available for patients undergoing cardiac surgery.
Objective: This brief communication seeks to explore the use of robotic technology to quantify distinctive patterns of visuospatial, sensorimotor, and cognitive functioning in patients undergoing TAVI.
Methods: Patients undergoing TAVI were recruited for this prospective observational study. Prior to their procedure, study participants performed four robotic reaching tasks using the Kinarm robotic system. Patients repeated the assessment three months after their TAVI procedure. Significant changes in overall task score and parameters were determined.
Results: Ten patients were recruited and included in this brief report. In a simple reaching task, patients show significant improvement in performance post-TAVI. However, patients do not improve nor worsen in a complex reaching task after TAVI. Similarly, patients demonstrate impairments in both trail making tasks before and after their TAVI procedure.
Conclusions: This study captures the variability in neurological functioning in older patients undergoing TAVI. Robotic technology and quantified assessment procedures can be extremely valuable for detecting perioperative neurological impairments in this patient population.

1. Introduction

Transcatheter aortic valve implantation (TAVI) is the recommended surgical procedure for patients with severe aortic stenosis and a greater risk of developing post-operative complications due to their older age or multiple comorbidities [1]. Patients undergoing TAVI present with similar mortality outcomes and repeat hospital admission rates compared to patients undergoing surgical aortic valve replacement [2]. However, TAVI patients may continue to experience post-operative cognitive decline 1–6 months after the procedure [3]. The cause of this decline in TAVI patients is likely multifactorial. Due to the high-risk nature of this patient population, pre-existing conditions such as renal dysfunction, prior stroke, and frailty may play a role in the development of post-operative cognitive impairment [3].

The majority of existing research on neurological functioning after TAVI utilize dementia screening tools such as the Mini-Mental State Examination (MMSE) or the Montreal Cognitive Assessment (MoCA) [4, 5]. Auffret and colleagues for example described functional declines in complex cognitive tasks involving executive functioning and processing speed in 25% of patients 30 days post-TAVI [5]. Using the MMSE,

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Schoenenberger et al. demonstrated global improvements in patients 6 months following TAVI [4]. However, these short-form assessments may not be able to detect more subtle pre-existing impairment, which may better predict long-term outcome post-operation [6]. Robotic technology has emerged as a more sensitive and objective measure of neurological function compared to pen-and-paper assessments [7,8]. An example of such technology is the Kinarm robotic platform (Kinarm, Kingston, Canada), which quantifies sensory, motor, and cognitive functioning using a standardized testing battery. This communication aims to examine the preliminary use of four Kinarm tasks to assess pre- and post-operative neurological functioning in 10 patients undergoing TAVI.

2. Material and methods

Adults undergoing TAVI were recruited for this prospective observational study conducted at the Kingston Health Sciences Centre. Informed consent was obtained for all participants during their pre-surgical screening appointment. This project was approved by the Health Sciences Research Ethics Board at Queen's University (DMED-1672–14). Patients were assessed using the Kinarm's Visually Guided Reaching (VGR), Reverse Visually Guided Reaching (RVGR), and Trail making tasks A and B (TMT-A and TMT-B) before and 3 months after TAVI. The Kinarm's experimental setup and its standardized tasks have been previously described [9] (see also www.kinarm.com). Robotic set-up and patient assessment was performed by a trained research associate. The following four tests included in this study took a total of 25 min to complete.

The VGR task quantifies basic visuospatial skills and sensorimotor control. With their hand position being represented by a white dot, participants were instructed to bring the white dot quickly and accurately to red targets as they appear. Successful performance involved making unassisted reaching movements from the central target to one of four peripheral targets and, when instructed, back to the central target [10]. In the RVGR task, the subject's movement is now reversed compared to the movement of the white dot on the screen. Patients are required to apply inhibitory control to prevent automatic reaching and executive functioning to bring the white dot to the red target by moving in the opposite direction. The trail-making tasks on the Kinarm involve the same attention and executive functioning as the classic test [11].

Task performance is quantified using temporal/spatial features of hand motion such as initial direction error, reaction time, and hand speed (Tables 2 and 3). Parameters are transformed into Z-space and corrected for age, handedness, and sex. The directionality of each parameter is manipulated so that positive values indicate poor performance, zero represents average performance, and negative values represent greater than average performance. At the 95% confidence level, parameters equal to 1.64 or greater denotes impairment. Performance in each task is also quantified using an overall task score. At the 95% confidence level, a task score of 1.96 or greater denotes impairment. Statistical changes in task scores and parameters were also determined using the confidence intervals, intraclass correlation coefficients, and learning effects derived by Simmatis et al [12]. For the purpose of this short communication, performance for each patient's dominant hand will be discussed. Data visualizations were created using R software [13].

3. Results

Ten patients aged 58–84 (mean: 75.4 ± 7.6) undergoing TAVI were recruited for this study. Due to insufficient time to complete their assessment, Patient 9 was not able to perform the TMT-A and TMT-B on the Kinarm before their TAVI. All other participants completed the four tasks presented in this report prior to their procedure. Three months after the operation, 8/10 patients returned to repeat the assessment. The remaining two patients (Patients 2 and 5) could not be reached for follow-up. Demographics and relevant comorbidities for each patient can be found in Table 1.

3.1. Improved performance observed in simple reaching task

Six out of the ten patients exhibited impaired performance on the VGR task score prior to surgery (Fig. 1). Each patient depicted unique performance patterns. Three months following their TAVI procedure, only Patient 7 was identified as impaired. There was a statistically significant improvement in performance on the VGR task for three of the other patients assessed at 3 months as compared to their pre-operative performance. Patient 8 was also identified as unimpaired post-TAVI, however this change was not significant.

Prior to TAVI, Patient 3 showed impairment in a variety of parameters, particularly in initial distance ratio (d) and speed maxima count (e). There was significant improvement in these parameters and others 3 months post-TAVI. Patient 5 depicted focal impairments in max speed (i) and no movement end (j). Patient 7 was also identified as impaired prior to TAVI, due to posture speed (a) and initial movement (c,d) parameters. Finally, Patients 6, 8, and 10 were very similar in their performance pattern, showing subtle impairment in reaction time (b), initial distance ratio (d), speed maxima count (e), min-max speed difference (f), movement time (g), path length ratio (h), and max speed (i).

3.2. Minimal significant change in overall performance in complex reaching task

Fifty percent of patients were identified as impaired on the RVGR task prior to their TAVI procedure (Fig. 2). Pre-operatively, Patient 1 depicted impairment in speed maxima count (g), movement time (i), and max speed (k). While Patient 1 significantly improved on reaction time (b), a similar pattern of impairment remained following their 3-month post-operative assessment. Patient 7 was also identified as impaired on the RVGR task prior to and after TAVI, despite significant improvements in initial direction angle (c).

Widespread impairment was observed in Patients 2 and 5 prior to surgery. Patient 2 was impaired in initial movement (c,d) and corrective movement (g,h) parameters, as well as movement time (i), path length ratio (j), and no movement end (l). Patient 5 performed poorly, specifically in the "no trial" parameters: no movement end (l) and no initial stabilization (m). The max speed (k), movement time (i), speed maxima count (g), and correction time (f) were also most affected.

For their pre-operative assessment, Patient 4 depicted subtle impairments in posture speed (a), correction time (f), speed maxima count (g), path length ratio (j), and no movement end (l) parameters. Three months post-TAVI, Patient 4 continued to perform the task outside of the normal range. In contrast, Patient 10 performed within the normal range before and after their TAVI procedure.

3.3. Variable changes observed in Trail making task performance

Fig. 3 shows perioperative performance of the Trail making task A (TMT-A). Four out of the nine (44%) patients who were assessed using the TMT-A were identified as impaired prior to TAVI. Post-operatively, Patient 7 improved in performance, testing within the normal range. However, Patients 3, 6, and 10 worsened and were identified as impaired, totaling to 6 out of 8 (75%) patients with task scores greater than 1.96. Patients 3 and 4 had significantly greater testing time (a) and dwell time (c), causing an overall significant decline in task performance (Task score > 1.96). Patient 10′s post-operative performance on TMT-A was also significantly worse compared to their pre-operative score, due to all-round impairment in testing time (a), time ratio (b), and dwell time (c). Finally, Patient 6 was also identified as impaired after TAVI due to subtle, non- significant changes in parameters.

Pre- and post-operative performance on the Trail Making Task B (TMT-B) is illustrated in Fig. 4. Five out of nine (55%) patients were

Table 1
Demographics and comorbidities for all ten patients included in this brief report. Y: Yes. N: No. COPD: chronic obstructive pulmonary disease.

	Demographics			Comorbidities/Patient History (7)							Total Comorbidities (*n*,% out of 7)
Patient ID	Age	Sex (M,F)	Non-white race (Y,N)	Hyper-tension (Y, N,%)	Type II Diabetes	Renal Dysfunction (Y, N,%)	Previous cardiac surgery (Y,N,%)	COPD/ Resp. dys. (Y,N,%)	Smoker	Alcohol Abuse	
1	82	M	N	N	Y	N	N	N	N	N	1, 14.3%
2	77	M	N	Y	Y	N	N	N	Y	N	3, 42.9%
3	72	F	N	Y	Y	N	Y	N	N	N	3, 42.9%
4	73	M	N	Y	N	N	Y	N	N	N	2, 28.6%
5	72	M	Y	N	N	N	Y	N	Y	N	2, 28.6%
6	58	F	N	Y	N	N	Y	Y	Y	Y	5, 71.4%
7	79	M	N	Y	N	Y	Y	N	N	N	3, 42.9%
8	84	M	N	Y	Y	N	N	N	N	N	2, 28.6%
9	83	F	N	Y	N	N	N	Y	N	N	2, 28.6%
10	74	M	N	Y	Y	N	Y	Y	N	N	4, 57.1%
Totals & Means	75.4 ± 7.6	7, 3	1, 9	8, 2	5, 5	1, 9	6, 4	3, 7	3, 7	1, 9	

Table 2
Parameters measured during the VGR and RVGR tasks. Parameters are grouped into 5 movement categories. Table adapted from the Kinarm user guide (Dexterit-E user guide version 3.8, Kinarm). * Indicates parameters only measured for the RVGR task.

MOVEMENT CATEGORY	PARAMETERS	DESCRIPTION
POSTURE CONTROL	Posture speed (a)	Hand speed when the hand should be a rest (median for all trials).
VISUAL REACTION	Reaction time (b)	Time between appearance of target and onset of hand movement (median for all trials).
INITIAL MOVEMENT	Initial direction angle (c)	Angular deviation between a straight line from the hand position at movement onset to the hand position after initial movement and a straight line from the hand position at movement onset to the target (median for all trials).
	Initial distance ratio (d)	Ratio of two distances travelled: 1. Distance of initial movement and 2. Distance between movement onset and offset (median for all trials).
	Direction errors* (RVGR: e)	Number of times the subject initially moved the cursor away from the target.
	Correction time* (RVGR: f)	For direction errors, this parameter is the mean time before the subject stated to move the cursor towards the target.
CORRECTIVE MOVEMENT	Speed maxima count (VGR: e; RVGR: g)	Number of hand speed maxima between movement onset and offset (mean for all trials).
	Min-max speed difference (VGR: f; RVGR: h)	The mean difference between pairs of adjacent hand speed minima and maxima, for all pairs between the time of max speed and movement offset (mean for all trials).
TOTAL MOVEMENT	Movement time (VGR: g; RVGR: i)	Total time elapsed from movement onset to offset.
	Path length ratio (VGR: h; RVGR: j)	Ratio of the distance travelled from movement onset to offset, and the straight line (direct) distance between them (mean for all trials).
	Max speed (VGR: i; RVGR: k)	Maximum hand speed achieved between movement onset and offset.
NO TRIAL	No movement end (VGR: j; RVGR: l)	Number of trials for which movement offset is not detected before the end of trial.
	No initial stabilization (VGR: k; RVGR: m)	Count of trials where the subject failed to stabilize at the starting target.

impaired during their baseline assessment. Of those five, four returned for their follow-up assessment after TAVI and continued to perform poorly. Patient 4 showed consistent impairment in both testing time (a) and dwell time (c) during pre- and post-operative assessments. Patient 8 significantly improved in performance after TAVI primarily due to a reduction in the dwell time (c) parameter. While there were other Patients (1 and 7) which showed significant changes in certain parameters such as testing time (a) and dwell time (b), this was not sufficient to impact overall task score or performance (Fig. 4).

Table 3
Parameters measured during the Trail making tests (A and B). Table adapted for the Kinarm user guide (Dexterit-E user guide version 3.8, Kinarm).

PARAMETERS	DESCRIPTION
Total time (a)	Total time from the targets being illuminated to touching the last target
Time of 2nd half/Time 1st half (b)	Total time for targets 13–25/total time for targets 1–13
Dwell time (c)	Total amount of time spent with the hand feedback dot at the targets

4. Discussion

This report highlights the preliminary use of robotic technology in detecting neurological impairments in older adults undergoing TAVI. In the VGR task, three patients significantly improved in performance three months after their TAVI procedure. In the RVGR task, one patient showed significant decline after TAVI, yet remained in the normal range. Similar patterns of performance were also observed before and after TAVI in the trail making tasks, where majority of patients who attended follow-up were identified as impaired. The Kinarm identified specific movement patterns responsible for impairment.

The Kinarm allows for more individualized and granular approach to neurological assessment compared to standardized pen-and-paper tests. Performance on each task can be described quantitatively through parameters that influence that overall task score. Certain patterns of performance before and after surgery can be determined by investigating changes in particular parameters. The Kinarm also measures overall neurological functioning by compiling motor, sensory, and cognitive performance to successfully complete certain tasks. Exploring changes in parameters can therefore aid in differentiating whether the impairment is either cognitively driven or rooted in sensorimotor functioning [14]. While the Kinarm has been an exceptionally valuable tool for research purposes, there may be obstacles in implementing such a thorough neurological assessment in a clinical setting. The entire battery of Kinarm Standard Tests can take between 1 and 1.5 h to complete. As well, the Kinarm robot is not easily portable, and requires a large space to be stored and used. However, there is immense benefit for the use of in-depth neurological assessments, particularly in a field where nature of impairment remains unclear. As with previous studies looking at

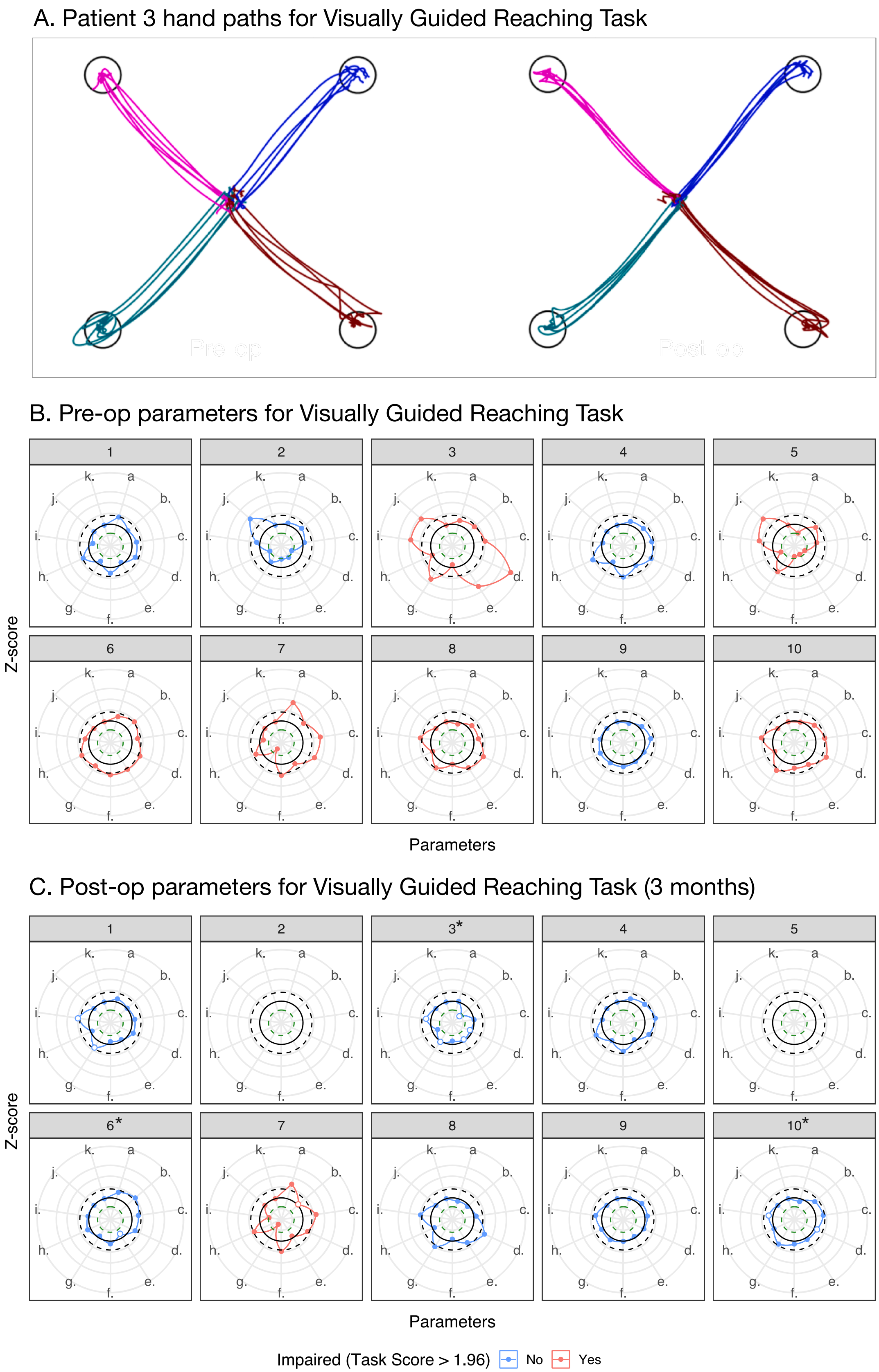

Fig. 1. A. Hand paths illustrating performance of Patient 3 on the Visually Guided Reaching (VGR) task before and 3 months after TAVI. Radar plots illustrating B. pre-operative and C. post-operative parameters on VGR. The area between the dashed lines represents average performance. Values greater than the black dashed line (1.64) signify impairment. Values less than the green dashed line (−1.64) signify greater than average performance. The solid black line represents zero on the plotting scale. *Denotes significant change in task score. Unfilled circles represent significant change in parameter value. Patients 2 and 5 did not participate in the 3-month assessment timepoint.

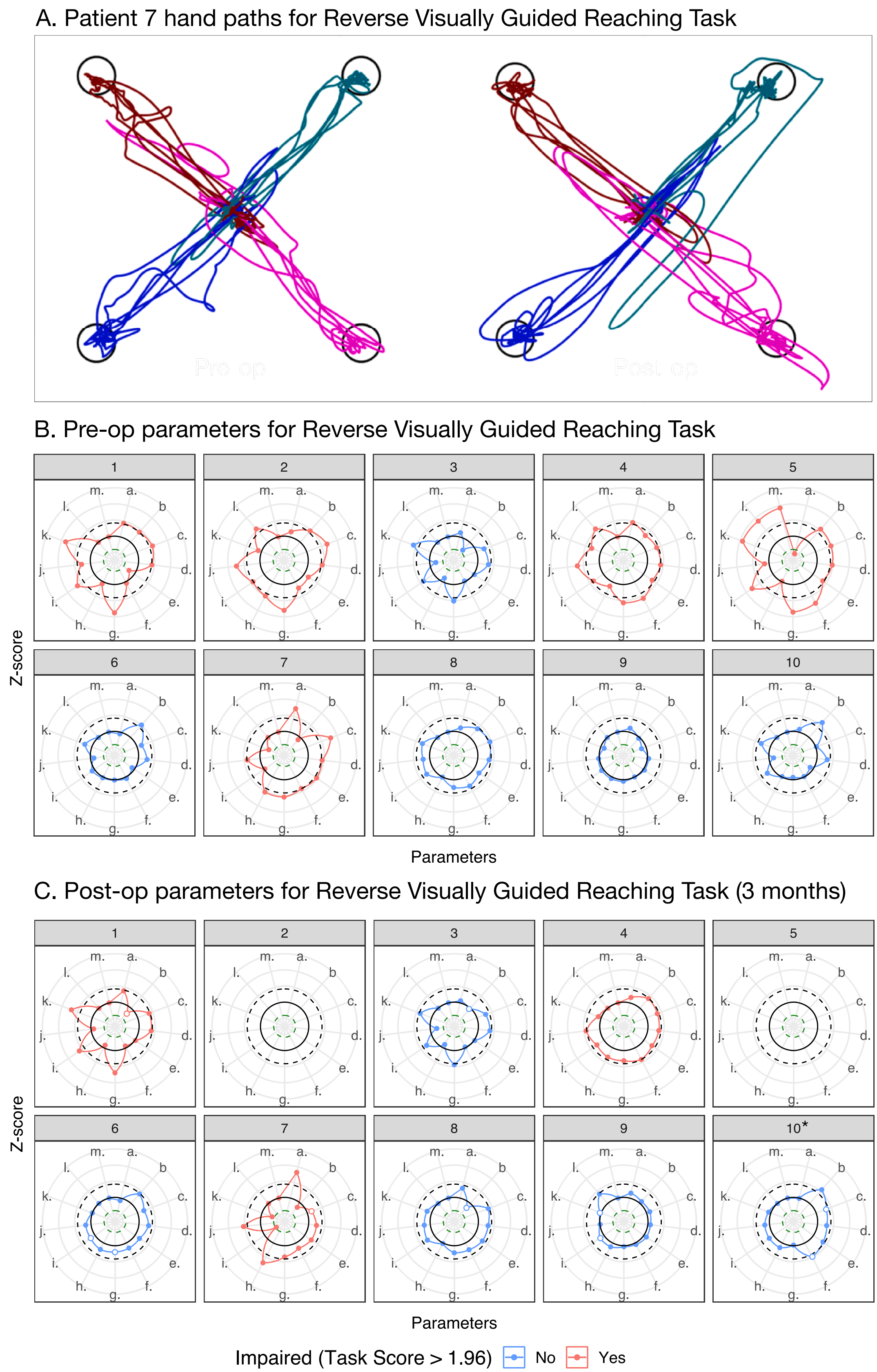

Fig. 2. A. Hand paths illustrating performance of Patient 7 on the Reverse visually guided reaching (RVGR) task before and 3 months after TAVI. Radar plots illustrating B. pre-operative and C. post-operative parameters on RVGR. The area between the dashed lines represents average performance. Parameters values greater than the black dashed line (1.64) signify impairment. Parameter values less than the green dashed line (-1.64) signify greater than average performance. The solid black line represents zero on the plotting scale. *Denotes significant change in task score. Unfilled circles represent significant change in parameter value. Patients 2 and 5 did not participate in the 3-month assessment timepoint.

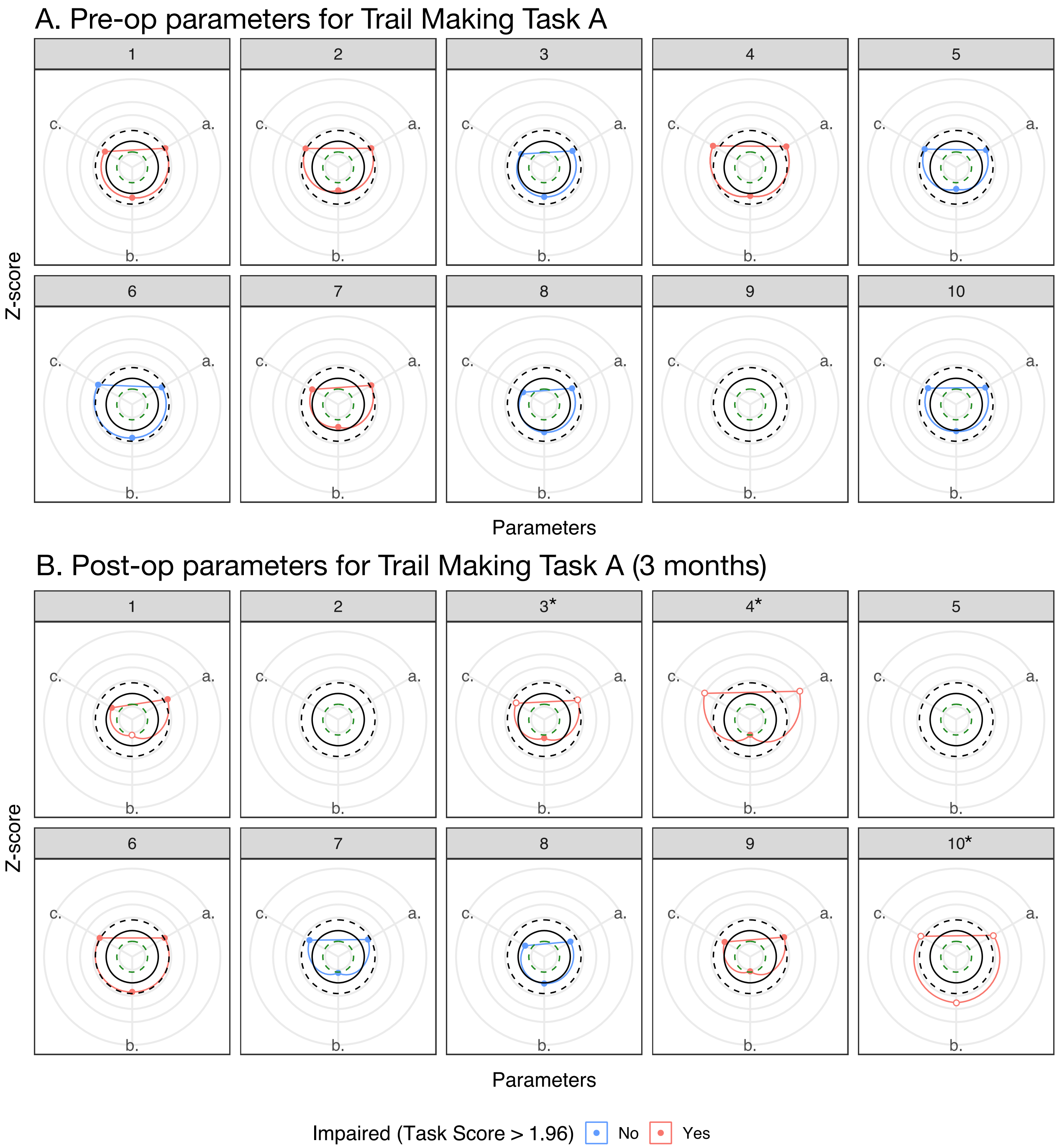

Fig. 3. Radar plots illustrating A. pre-operative and B. post-operative parameters on the TMT-A task. The area between the dashed lines represents average performance. The black dashed line represents 1.64 on the plotting scale. The green dashed line represents -1.64 on the plotting scale. The solid black line represents zero on the plotting scale. *Denotes significant change in task score. Unfilled circles represent significant change in parameter value. Patient 9 was not available to complete the trail making task prior to their TAVI procedure.

Kinarm performance after stroke, the goal of this study was to explore individual differences that can present within a patient population [15, 16]. The nature of impairment in any clinical cohort can be extremely diverse and can direct the form of care they receive. Likewise, the perioperative neurological complications experienced by patients undergoing TAVI can vary greatly, suggesting that routine assessment should become a part of individualized care.

The findings from this study were primarily descriptive, yet they suggest that neurological assessment prior to surgery can provide valuable information about a patient's functioning post-operation. Demographic and comorbidity data varied greatly among the ten patients, highlighting the unique and multifactorial nature of neurological decline in this high-risk patient population [17]. For example, while Patient 6 was younger than Patient 4, they presented with 3 more comorbidities. Early improvements in cognitive function have been reported after TAVI using standardized testing batteries [18]. However, with this small sample of patients, there was only substantial improvement with VGR, a simple motor reaching task. In contrast, more cognitively demanding tasks, such as RVGR, TMT-A, and TMT-B, showed higher rates of impairment before and after TAVI. This does

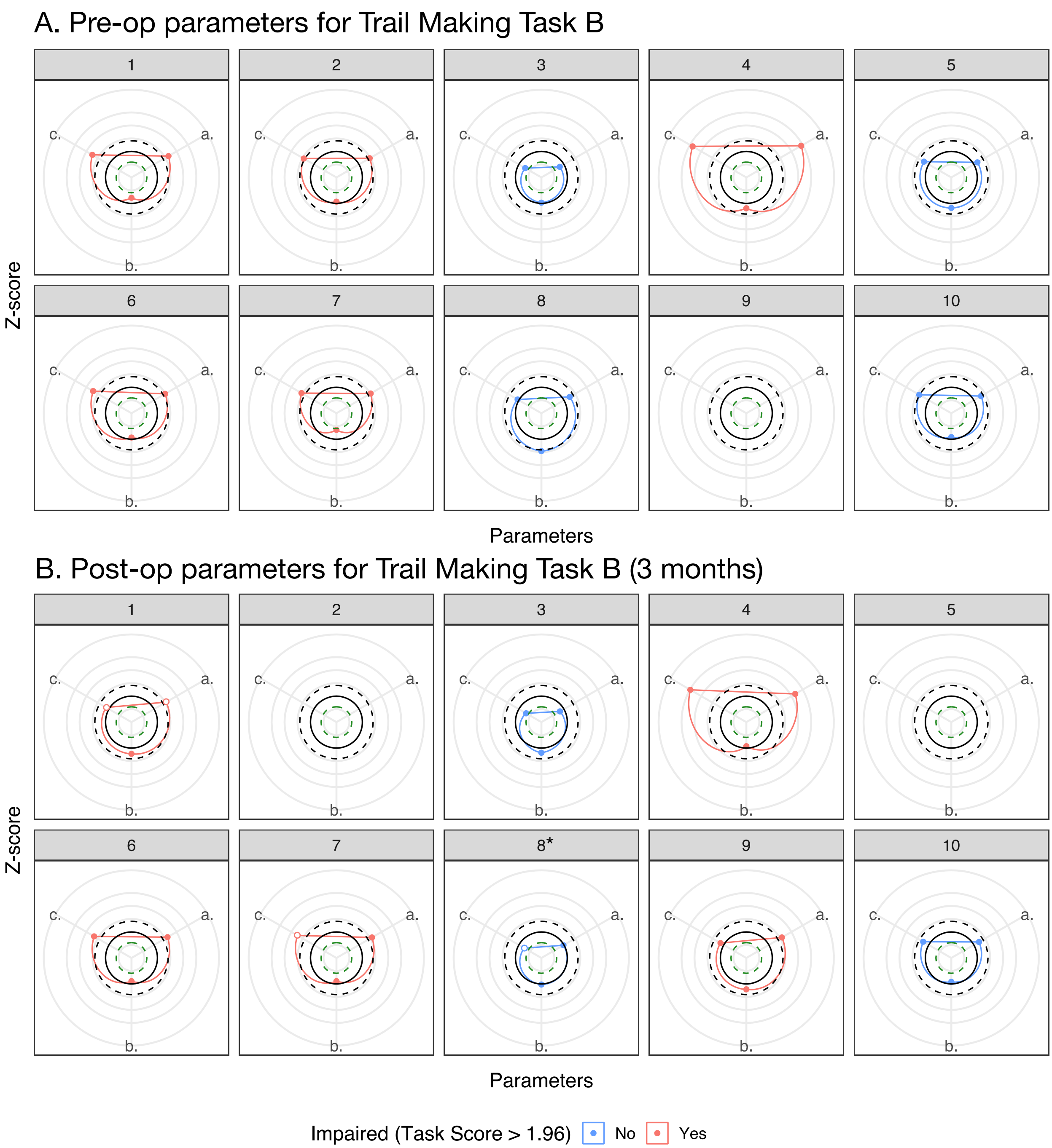

Fig. 4. Radar plots illustrating A. pre-operative and B. post-operative parameters on the TMT-B task. The area between the dashed lines represents average performance. The black dashed line represents 1.64 on the plotting scale. The green dashed line represents -1.64 on the plotting scale. The solid black line represents zero on the plotting scale. *Denotes significant change in task score. Unfilled circles represent significant change in parameter value. Patient 9 was not available to complete the trail making task prior to their TAVI procedure.

suggest that performance on certain complex tasks prior to surgery can provide valuable information about a patient's cognitive state post-operation. Other studies have also emphasized the importance of pre-operative screening in high-risk patients undergoing TAVI, suggesting that baseline cognitive impairment and frailty can predict delirium after surgery [19].

5. Conclusions

The objective of this study was to explore how objective neurological testing can improve our understanding of perioperative impairment in high-risk/older populations. However, two patients who performed poorly on the tasks pre-TAVI did not return for their follow-up assessment. Nevertheless, this brief report does highlight the benefits of quantifying perioperative neurological impairment in patients undergoing TAVI. Including additional neurological tasks as well as assessment timepoint in larger cohorts will help identify potentially significant group differences in recovery. Future studies will be sufficiently powered to confirm these findings and determine predictors of impairment.

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Declaration of Competing Interest

JSS, AGH, DP, DMP, GB, and TS have nothing to disclose. SHS is the inventor of the Kinarm robot and co-founder of its distribution company, Kinarm. JGB receives a stipend for the Trillium of Life Network for his role as a hospital donation physician.

References

[1] P. Ponikowski, A.A. Voors, S.D. Anker, H. Bueno, J.G.F. Cleland, A.J.S. Coats, et al., 2016 ESC Guidelines for the diagnosis and treatment of acute and chronic heart failure, Eur. Heart J. 37 (27) (2016) 2129–2200, https://doi.org/10.1093/eurheartj/ehw128.

[2] M.J. Mack, M.B. Leon, C.R. Smith, C. Miller, J. Rey, W. Moses, et al., 5-year outcomes of transcatheter aortic valve replacement or surgical aortic valve replacement for high surgical risk patients with aortic stenosis (PARTNER 1): a randomised controlled trial, Lancet 385 (2015) 2477–2484, https://doi.org/10.1016/S0140-6736(15)60308-7.

[3] E.S. Ghezzi, T.J. Ross, D. Davis, P.J. Psaltis, T. Loetscher, H.A.D. Keage, Meta-analysis of prevalence and risk factors for cognitive decline and improvement after transcatheter aortic valve implantation, Am. J. Cardiol. 127 (2020) 105–112, https://doi.org/10.1016/j.amjcard.2020.04.023.

[4] A.W. Schoenenberger, C. Zuber, A. Moser, M. Zwahlen, P. Wenaweser, S. Windecker, et al., Evolution of cognitive function after transcatheter aortic valve implantation, Circ. Cardiovasc. Interv. 9 (2016), e003590, https://doi.org/10.1161/CIRCINTERVENTIONS.116.003590.

[5] V. Auffret, F. Campelo-Parada, A. Regueiro, M. Trigo Del, O. Chiche, C. Chamandi, et al., Serial changes in cognitive function following transcatheter aortic valve replacement, J. Am. Coll. Cardiol. 68 (20) (2016) 2129–2141.

[6] H.C. Lingehall, N.S. Smulter, E. Lindahl, M. Lindkvist, Preoperative cognitive performance and postoperative delirium are independently associated with future dementia in older people who have undergone cardiac surgery, Crit. Care Med. 45 (8) (2017) 1295–1303, https://doi.org/10.1097/CCM.0000000000002483.

[7] S.H. Scott, S.P. Dukelow, Potential of robots as next-generation technology for clinical assessment of neurological disorders and upper-limb therapy, J. Rehabil. Res. Dev. 48 (4) (2011) 335, https://doi.org/10.1017/CBO9781107415324.004.

[8] A. Schwarz, C.M. Kanzler, O. Lambercy, A.R. Luft, J.M. Veerbeek, Systematic review on kinematic assessments of upper limb movements after stroke, Stroke 50 (3) (2019) 718–727, https://doi.org/10.1161/STROKEAHA.118.023531.

[9] J.S. Semrau, S.H. Scott, A.G. Hamilton, D. Petsikas, D.M. Payne, G. Bisleri, et al., Road to recovery: a study protocol quantifying neurological outcome in cardiac surgery patients and the role of cerebral oximetry, BMJ Open 9 (12) (2019) 1–6, https://doi.org/10.1136/bmjopen-2019-032935.

[10] A.M. Coderre, A.M. Abou Zeid, S.P. Dukelow, M.J. Demmer, K.D. Moore, M. J. Demers, et al., Assessment of upper-limb sensorimotor function of subacute stroke patients using visually guided reaching, Neurorehabil. Neural Repair 24 (6) (2010) 528–541, https://doi.org/10.1177/1545968309356091.

[11] C.R. Bowie, P.D. Harvey, Administration and interpretation of the trail making test, Nat. Protoc. 1 (5) (2006) 2277–2281, https://doi.org/10.1038/NPROT.2006.390, 2006 15.

[12] L.E.R. Simmatis, S. Early, K.D. Moore, S. Appaqaq, S.H. Scott, Statistical measures of motor, sensory and cognitive performance across repeated robot-based testing, J. Neuroeng. Rehabil. 17 (1) (2020) 86, https://doi.org/10.1186/s12984-020-00713-2.

[13] R Core Team. R: A language and environment for statistical ## computing, R Foundation for Statistical Computing, Vienna, Austria, 2021.

[14] S.H. Scott, S.P. Dukelow, Potential of robots as next-generation technology for clinical assessment of neurological disorders and upper-limb therapy, J. Rehabil. Res. Dev. 48 (4) (2011) 335–354, https://doi.org/10.1682/JRRD.2010.04.0057.

[15] C.R. Lowrey, C.P. Jackson, S.D. Bagg, S.P. Dukelow, S.H. Scott, A novel robotic task for assessing impairments in bimanual coordination post-stroke, Int. J. Phys. Med. Rehabil. S3 (2014) 002, https://doi.org/10.4172/2329-9096.S3-002.

[16] S.P. Dukelow, T.M. Herter, K.D. Moore, M.J. Demers, J.I. Glasgow, S.D. Bagg, et al., Quantitative assessment of limb position sense following stroke, Neurorehabil. Neural Repair 24 (2) (2010) 178–187, https://doi.org/10.1177/1545968309345267.

[17] N.E. Moat, P. Ludman, M.A. de Belder, B. Bridgewater, A.D. Cunningham, C. P. Young, et al., Long-term outcomes after transcatheter aortic valve implantation in high-risk patients with severe aortic stenosis the U.K. TAVI (United Kingdom Transcatheter Aortic Valve Implantation) registry, JAC 58 (20) (2011) 2130–2138, https://doi.org/10.1016/j.jacc.2011.08.050.

[18] M.M. Khan, N. Herrmann, D. Gallagher, D. Gandell, S.E. Fremes, H. C. Wijeysundera, et al., Cognitive outcomes after transcatheter aortic valve implantation: a metaanalysis, J. Am. Geriatr. Soc. 66 (2) (2018) 254–262, https://doi.org/10.1111/jgs.15123.

[19] M.M. Khan, K.L. Lanctôt, S.E. Fremes, H.C. Wijeysundera, S. Radhakrishnan, D. Gallagher, et al., The value of screening for cognition, depression, and frailty in patients referred for TAVI, Clin. Interv. Aging 14 (2019) 841–848, https://doi.org/10.2147/CIA.S201615.