FACULDADE DE MEDICINA DA UNIVERSIDADE DE COIMBRA

MESTRADO INTEGRADO EM MEDICINA – TRABALHO FINAL

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Impact of multiple surgeries with associated infection episodes on cognitive dysfunction

ARTIGO CIENTÍFICO

ÁREA CIENTÍFICA DE PSIQUIATRIA

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MARÇO/2017

FACULDADE DE MEDICINA DA UNIVERSIDADE DE COIMBRA

Impact of multiple surgeries with associated infection episodes on cognitive dysfunction

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Abstract

Background: Mild cognitive impairment is an intermediate clinical state between healthy aging and dementia. On the postoperative period, subtle cognitive dysfunction is a commonly reported problem, however there are controversial reports on the influencing factors of this decline. This study investigated the presence of cognitive decline on a Portuguese population with past history of established infection and repeated surgeries.

Material and Methods: Thirty-two patients with mean age of 71 years old with a diagnosed periprosthetic infection and that underwent at least two surgeries were studied in a cross-sectional study. Evaluation consisted of a battery of tests: Montreal Cognitive Assessment (MoCA), Frontal Assessment Battery (FAB), Subjective Memory Complaints Scale (SMC), Geriatric Depression Scale-30 (GDS-30) and Instrumental Activity of Daily Living (IADL) and it was applied between 1 to 84 months after the last surgery. All the participants completed at least one of the tests and cognitive function was assessed using the MoCA test. Results were compared with the ones from a Portuguese reference population, matched for age and educational level.

Results: MoCA results (19.8 ± 3.83) were significantly lower (one-tailed T test, p=0.005) compared to data from the reference population (21.9 ± 3.20), GDS was not significantly different, even though a case of severe depression was detected. FAB results were not significantly different from the reference population, while the study group performed better on the SMC test (one-sample Wilcoxon Signed Rank test, p<0.001). The IADL test detected severe dependency on 2 subjects (6.2%) and moderate dependency on 1 subject (3.1%).

Conclusions: Lower cognitive levels, assessed by the MoCA test, were detected on patients submitted to multiple orthopaedic surgeries with associated periprosthetic infection compared to the reference population. Since a defined methodology to detected cognitive decline on the postoperative period is lacking, the MoCA test was chosen for evaluation, which is a screening tool with good parametric values to detect mild cognitive impairment stages. Executive dysfunction was not found, however IADl detected cases of severe and moderate dependency suggesting a decreased cognitive function. SMC results were surprisingly better compared to the reference population. There seems to be an association between repeated surgeries with associated infection episode and cognitive decline.

Keywords

Cognitive dysfunction, Surgical procedures, Anaesthesia, Infection, Neuropsychological tests

Introduction

Mild Cognitive Impairment (MCI) represents a clinical state in which subtle cognitive impairment is observed as compared to healthy aging. The diagnostic criteria according to the Mayo Clinic Key Symposium are: (1) cognitive complaints raised by the patient or their families, (2) cognitive decline reported on a clinical evaluation, (3) absence of dementia and (4) absence of major repercussions on daily life activities. Experiencing difficulties in performing complex tasks on daily life are accepted.[1] MCI may represent the first clinical state of a degenerative process, therefore the importance of an early diagnosis, as it may allow to detect the people at a higher risk of progression to dementia.[2]

Multiple aetiologies have been described to cause cognitive decline. On the postoperative period, a subtle cognitive impairment was described.[3,4] The concept of postoperative cognitive dysfunction (POCD) is commonly used and characterized as a new decline in the cognitive faculties after a surgical procedure. Memory, concentration, and information process are the domains that have been primarily associated with this profile. There is not yet a formal psychiatric diagnosis; however, it is different from delirium or dementia, and it is considered a type of MCI.[5,6] Being a discrete process, the cognitive decline may only be detected by the patient or partner once daily life is resumed.[7]

POCD was initially reported as a cardiac surgery complication; later it was also associated with non-cardiac surgeries. A controlled longitudinal study, with 355 participants older than 60 years old, detected cognitive dysfunction in 12.7% 3 months after surgery.[3]

The physiopathology of POCD is unclear, but it is likely that inflammatory pathways are involved.[8] The triggers for POCD may be multifactorial and multiple risk factors were established. POCD affects all ages at hospital discharge, though only the elderly population presents significant impairment 3 months after surgery. Lower educational level, previous stroke without cognitive impairment, POCD diagnosed at hospital discharge[3] and a reduced preoperative cognitive reserve are predisposing factors for POCD. Alcohol abuse and a depressive basal mood is also an established risk factor.[9]

The role of anaesthesia on the development of POCD has been studied and a higher incidence of POCD using general anaesthesia when compared to regional anaesthesia was not found.[10,11]

There are contradictory results regarding the risk that a second surgery represent on cognitive function. The International Multicentre Study on long-term Postoperative Cognitive Dysfunction (ISPOCD1) registered an incidence of POCD of 14% 3 months after surgery with a second surgery process. An association with infectious process was also found, but it was only significant at POCD detected one week after surgery.[12] On the another hand, Monk *et al* found no association between second surgery and a higher incidence of POCD.[3]

POCD is associated with a bigger risk of death within one year after surgery[3,4], of early retirement and greater utilisation of social support, increased morbidity[12], delayed functional recovery in the early and late postoperative period up to the rehabilitation phase, suggesting that POCD is a serious complication with life threatening implications.

Life expectancy is increasing, motivating a rise in the number of elderly people undergoing surgery and leading to an increased rate of cognitive impairment on the postoperative care.[7,13]

There is no knowledge of a previous study in Portugal reporting cognitive decline after surgery. Cognitive impairment was reported on the follow-up of orthopaedic procedures[3,12] and a similar prevalence in fast-track surgeries and elective procedures at a 3-month period is documented.[14]

Nevertheless, it is yet not clear whether multiple surgeries and infection process are a significant risk for developing POCD.

The primary aim of this study was to identify the presence of decline in the general cognitive status defined by the Montreal Cognitive Assessment (MoCA) in an elderly population submitted to multiple surgeries and general anaesthesia with extensive associated infection episode in comparison with values from the matched Portuguese reference population. In addition, we sought to characterize the population in study using the battery of tests: Frontal Assessment Battery (FAB), Subjective Memory Complaints Scale (SMC), Geriatric Depression Scale (GDS) and Instrument of Activity of Daily Living (IADL).

Materials and methods

This cross-sectional observational study was conducted in Centro Hospitalar Universitário de Coimbra (CHUC), Department of Orthopedics during a twelve-month period, from February 2016 to February 2017. The subgroup analysis was gathered from the patients registered on the Orthopaedic Department who were submitted to a knee surgery between 2009 and 2016. The patients were recruited to participate in the study and informed consent was obtained from each patient.

Additional inclusion criteria included: (1) established periprosthetic joint infection on the follow-up of an elective total joint arthroplasty (TJA), (2) patient being submitted to at least a second knee surgery, (3) the last surgery taking place more than 1 month before evaluation and (4) having Portuguese as native language.

A periprosthetic joint infection is defined by one positive major criteria: two positive periprosthetic cultures with phenotypically identical organisms, or a sinus tract communicating with the joint, or the presence of three of the following minor criteria: elevated serum C-reactive protein (CRP) and erythrocyte sedimentation rate (ESR); elevated synovial fluid white blood cell (WBC) count or positive change on leukocyte esterase test strip; elevated synovial fluid polymorphonuclear neutrophil percentage; positive histological analysis of periprosthetic tissue or a single positive culture.[15]

Patients with established diagnosis of: Central Nervous Lesion, Dementia, Development disorders or Major Depression were excluded. Severe hearing or reading impairment and illiteracy also constituted excluding criteria. Patients with severe depression detected by the GDS-30 were excluded from MoCA and FAB analysis.

As sociodemographic data, we evaluated: age, gender, education level and medical history. A detailed history of past surgical procedures was gathered, including all previous surgeries, dates, type of anaesthesia, duration of anaesthesia. Regarding the TJA, the surgical indication, the hospital where the surgery was performed, complications, duration of hospital postoperative stay were listed. Clinical data were recorded from the patients and complemented with the medical records.

Patients were first evaluated on an orthopaedic consultation where pain and inflammatory signs from the knee were registered and the Lower Extremity Functional Scale (LEFS) was fulfilled.

Neuropsychological Assessments:

Two investigators carried out neuropsychological assessments. The tests were applied in the same sequence as mentioned, except for the tests FAB and MoCA, whose order was randomly inverted.

Geriatric Depressive Scale (GDS)

Depressive symptoms were screened using the GDS. It is a yes/no questionnaire with 30 items that concerns feelings and behaviours within the last week. The score ranges from 0 to 30. It has a superior sensitivity (84%) and specificity (95%) for detecting depression, when compared to the shorter version.[16,17] The GDS scale was translated and applied to the Portuguese population and was previously used to detect depression in other cognitive studies.[18,19]

Subjective Memory Complaints Scale (SMC)

The concern regarding a change in cognition was evaluated using the SMC. It is a brief test with 10 questions, where the score ranges from 0 to 21 and assess subjects' perception of changes in memory. This scale has been validated for the Portuguese population.[20,21]

The Montreal Cognitive Assessment (MoCA)

The MoCA test is a cognitive screening tool developed to screen for MCI. It is a one-page document with 30 items that assesses 8 different domains: executive functions, temporal and spatial orientation, visuospatial abilities, short-term memory, working memory, language, attention and concentration.[22] It was translated and adapted to the Portuguese population, and normative cut-off values for Minimal Cognitive Impairment were established. The values are established according to age (25 to 49, 50 to 64 and over 65 years old) and education level (primary, middle, high and university).[19]

Frontal Assessment Battery (FAB)

FAB is a test with good psychometric properties to evaluate frontal lobe functions. It comprises 6 tasks, from these: Similarities, Go-No-Go and Fluency present the highest discrimination. The duration of application is on average 10 minutes. Normative data per age (20-39, 40-59, 60-79 and more than 80 years old) and level of education (1-3 years, 4-6 years, 7-12 years and more than 12 years) was established for the healthy Portuguese population. [23]

Instrumental Activity of Daily Living (IADL)

The Lawton Instrumental Activity of Daily Living (IADL) is an appropriate instrument to assess independent living skills.[3] Seven items are assessed: the ability to use the telephone, go shopping, prepare food, do the housekeeping, do the laundry, use of transportation, responsibility for own medications and ability to handle finances. It ranges from 0-5 in males and 0-8 in females, as not all tasks are registered in males.[24] The Portuguese version has been validated and used previously.[25]

Statistical Analysis

Data obtained from the collected sample are compared with the normative values from matched Portuguese population, stratified per age and educational category.

The normality of the variables MoCA, FAB, SMC and GDS was assessed using a Shapiro-Wilk test. The one-sample T-test was used to compare the results from MoCA, FAB and GDS with reference values. We resorted to a one-sample Wilcoxon Signed-Rank test to determine whether the SMC results differ from the reference values. For all tests, we used the mean value of the reference population. [19,23]

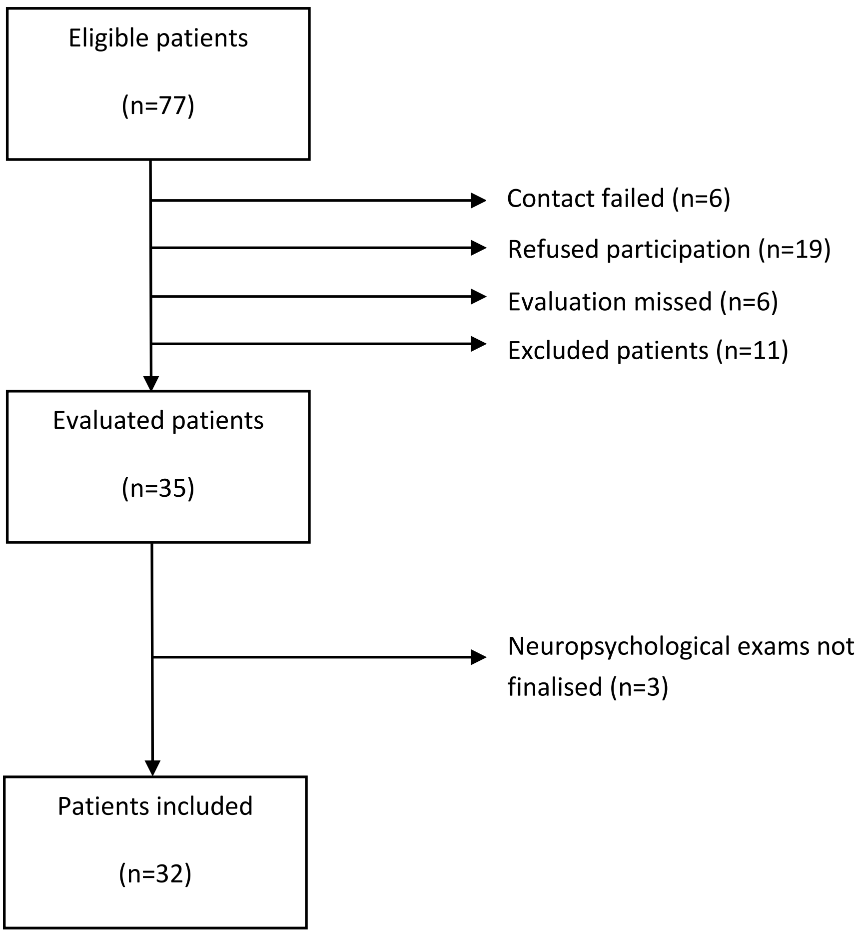
Statistical analyses were performed using the SPSS for Windows 22.0 (SPSS, IBM, USA) and a significance level of 0.05 was set for all statistical tests.

Results

Patient Cohort

A total of 77 patients were assessed for eligibility. Contact failed in 6 patients, 19 refused to participate, 6 missed the evaluation and 11 were excluded (3 due to diagnosis of major depression, 1 due to Parkinson diagnosis, 1 due to diagnosis of dementia, 2 due to previous stroke, 2 were hospitalised and 2 were waiting surgery). Therefore, a total of 35 patients signed the informed consent; 3 more were afterwards excluded because they failed to complete any neuropsychological exams. The MoCA test was completed by 29 individuals and 2 were excluded from analysis due to severe depression detected on the GDS-30. (Fig. 1).

FIGURE 1 - FLOW DIAGRAM OF PATIENTS SELECTION.



Demographics

The mean age was 71.2 ± 6.7 with a range of 54 to 89 years. There were 17 males and 15 females. The distribution of the education level was as follows: 27 patients (84.4%) patients with an education of 1-4 years, 4 patients (12.5%) with an education from 5 to 9 years and 1 (3.1%) with an education of 10-12 years. (Table 1). Patient comorbidity and surgery data are presented below. (Tables 2 and 3). All patients were submitted to a TJA due to osteoarthritis. Twenty-seven patients were submitted to an Arthrodesis with Compressive External Fixation and 26 of the procedures were performed with the use of general anaesthesia. All patients reported at the time of evaluation clinically meaningful functional change (>9) evaluated with the LEFS.

Table 1. Patients demographic data

Demographic data	No. of patients	Mean
Age (years) (median, IQR)	32	71.2 ± 6.75 (54-89)
Gender male/female	17/15	
Education level		
1-4 years	27	
5-9 years	4	
10-12 years	1	

Table 2. Patient Comorbidity

Medical History	No. of patients, n (%)
Psychiatry Disease	1 (3.1)
Neoplasia	3 (9.4)
Diabetes Mellitus	11 (34.4)
Cardiac Disease	11 (34.4)
Pulmonary Disease	2 (6.3)
Hepatic Disease	1 (3.1)
Kidney Disease	2 (6.3)
Systemic Disease	1 (3.1)
Rheumatic Disease	7 (21.9)
Disease with prolonged fever	1 (3.1)
Chronic Disease (lasting 1 month or more)	5 (15.6)

Table 3. Surgical data and clinical evaluation

Surgeries	
Number of surgeries per patient (mean ± SD, IQR)	6.5 ± 2.58 (2-12)
On Knee with Prosthesis (mean ± SD, IQR)	4.7 ± 2.05 (2-11)
Number of patients with arthrodesis (n, %)	27 (84.4)
Number of patients with rearthrodesis (n, %)	9 (28.1)
With General Anaesthesia (mean ± SD, IQR)	6.0 ± 2.30 (2-11)
Risk Factors for Infection (mean ± SD, IQR)	1.8 ± 1.10 (0-4)
Time between evaluation and last surgery (months) (mean ± SD, IQR)	30.8 ± 25.95 (1-84)
Lower Extremity Functional Scale (mean ± SD, IQR)	34.5 ± 8.67 (17-55)
Presence of pain (n, %)	8 (25)
Local Inflammatory Signs	9 (28.1)

Neuropsychological assessments

Neuropsychological assessment was performed within a range of 1 to 84 months after the last surgery. Test results are shown in Tables 4 to 6.

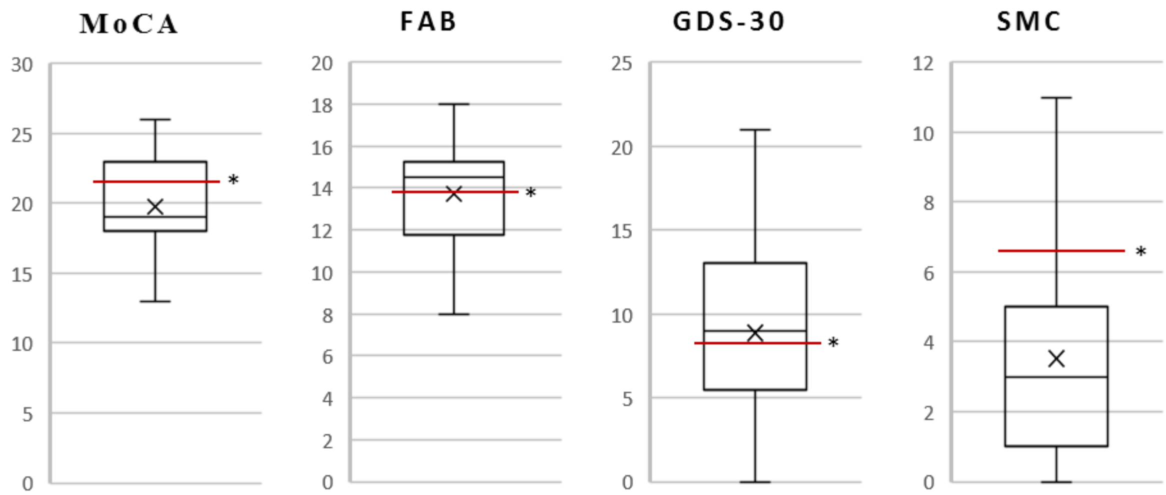
The mean MoCA score observed in the 27 patients included was significantly different from the mean score of the reference population, (one-tailed T-Test t(26)=-2.767, *p*=0.005).[19] GDS-30 and FAB results were not statistically different from the reference population, (two tailed T-Test; t(31)=1.261, *p*=0.217 and t(31)=0.331, *p*=0.743 respectively). SMC results were significantly lower (two-tailed Wilcoxon Signed Rank Test p<0.001) compared with the mean of the reference population (6.4 ± 3.40). Severe depression was found in 2 subjects (6.3%), severe dependency in 2 subjects (6.3%) and moderate dependency was detected in 1 subject (3.1%).

Table 4. Tests results

	Present study		Reference population	
Test	**No. patients**	**Mean ± SD**	**Mean ± SD**	***p*-value**
MoCA	27	19.8 ± 3.83	21.9 ± 3.20	0.005*
FAB	28	13.6 ± 3.20	13.4 ± 2.48	0.743
GDS-30	32	8.7 ± 5.44	7.4 ± 5.19	0.217
SMC	32	3.4 ± 3.05	6.4 ± 3.40	p<0.001

*one-tailed T-Test

Figure 2. Neuropsychological tests results compared with reference population



*Mean of reference population

Table 5. GDS and SMC scores distribution

GDS-30	
No depression (0-10)	22 (68.8)
Mild depression (11-20)	8 (25.0)
Severe depression (21-30)	2 (6.3)
SMC	
Without complaints (<3)	18 (56.3)
Complaints (>3)	13 (43.8)

Table 6. IADL scores distribution

	Female		Male	
	Cut-off	**n (%)**	**Cut-off**	**n (%)**
Total dependency	0-1	0	0	0
Severe dependency	2-3	1 (6.7)	1	1 (5.9)
Moderate	4-5	0	2-3	1 (5.9)
Mild dependency	6-7	0	4	0
Independent	8	14 (93.3)	5	15 (88.2)
Total		15		17

Discussion

In this study, we evaluated the presence of cognitive decline on an elderly population (mean of 71 years old) submitted to a minimum of two prosthetic knee surgeries, using a well-recognised test, and data from an age and education level matched healthy reference population. Statistically significant lower results on the MoCA test were observed on the subjects compared to the reference population (one-tailed T-test, P=0.005).

Cognitive impairment on hospital discharge clearly has been reported with rates up to 40%; however, whether cognitive dysfunction is a long-lasting consequence is still controversial.[7,26] A meta-analysis on cognitive decline on TJAs follow-up, showed no significant decline on the late postoperative period. However, it is pointed out that the application of tests with lower sensitivity, such as the Mini Mental State Exam (MMSE), that improvements on repeated tests and group data may have masked significance of results.[13]

Our finding is supported by other authors, who also detected a significant mild cognitive decline on late postoperative period. The largest study evaluating POCD is the ISPOCD1. This study included numerous patients submitted to knee replacement. At a 3-months evaluation, cognitive decline was reported on orthopaedic patients with an incidence of 10.8% (31 of 287).[12] A systematic review reported an overall incidence of POCD after noncardiac surgery of 11.7% on adults (age ≥18 years old) and established increasing age as the most important variable.[27] Nevertheless, the impact of multiple surgeries was not previously reported. We found that patients undergoing multiple surgeries perform lower on cognitive tests.

At hospital discharge, surgery complexity and a higher opioid analgesic usage are predictors of a higher POCD. The use of opioid analgesics and heightened level of pain influences the performance on neurocognitive tests.[3,13] This confers more reliability to data recorded on later periods; in order to prevent this bias. Thus, we used a minimum interval of 1 month between last surgery and cognitive evaluation with a mean of 31 months.

There is not a defined methodology for the diagnosis of cognitive dysfunction on the postoperative period.[6] Despite the different methodology our results are in accordance with previous studies. In our study we used the MoCA test, a tool developed to screen for mild cognitive impairment stages with higher sensitivity (81%) when compared to the MMSE, used on previous studies.[7,13,28] On the other hand, a duration of application of 10 minutes makes it more suitable to a clinical context, when compared to a more extensive battery of tests. The MoCA test has been successfully used on recent studies to evaluate mild cognitive dysfunction.[19,29,30]

SMC results were surprisingly lower than the ones from the reference population. Lack of subjective memory complaints on patients with low cognitive status have been attributed to loss of insight and metacognition, a common characteristic of both dementia and mild cognitive impairment and also to the presence of cognitive decline attributed to domains other than memory.[31]

Executive dysfunction on this group was not suggested by the FAB outcomes.[23]

IADL detected severe dependence in 3 subjects, of those, 2 failed to complete the MoCA test and 1 presented very low scores (13). These results are consistent with the literature. Loss of independence and ability to perform daily tasks is suggestive of cognitive impairment or even dementia.[2] Moreover, low scores on the IADL test have been described in patients with MCI diagnosis[32] and also after surgical insult.[33]

In our study, GDS-30 was used to screen for depression. The scores obtained were not significantly different from the reference population, however severe depression was found in two subjects, who were afterwards excluded from the MoCA and FAB analysis. The exclusion of major depression is widely applied on neurocognitive studies, as a depressive state may produce a false positive result on the evaluating test. However, mild depression may be accepted.[2,19,22]

Consistent with our results, a recent controlled trial has presented a significant higher prevalence on short-term cognitive impairment comparing subjects performing first surgery with subjects who had already undergone previous multiple surgeries.[34] Long-term evaluation is however missing. These findings are in line with the theory of cognitive reserve, which suggests that previous brain insults may increase susceptibility for cognitive impairment manifestations.[6,7] Moreover, a research studying the impact of pre-existing cognitive impairment on postoperative cognitive decline found a strong positive correlation.[35]

Associated infection in these patients may have been a risk factor for cognitive decline;[7] moreover, it is known that the elderly represent the most susceptible age range for postoperative complications.[26] In accordance, a research has observed increased rates of cognitive decline after sepsis insult.[36] This is consistent with the hypothesis of inflammation on the pathogenesis of cognitive dysfunction. Preclinical models describe that increased systemic inflammatory molecules induce neuroinflammation, along with impairment of the blood-brain barrier permeability leading to macrophage activation and parenchyma infiltration, particularly on the hippocampal region.[8]

Illiterate participants were excluded, as multiple items on the MoCA test require literacy abilities. This is in accordance with the criteria used for the Portuguese normative values.[19] This decision, along with excluding subjects with dementia and severe depression may have contributed for underestimation of the cognitive decline due to surgical impact, since these participants may represent the most vulnerable ones.[19,26] An additional factor may have been the patients who failed the evaluation due to impairing physical or mental disability.

This study should be considered in light of certain limitations. Firstly, the small size of the sample may hinder the generalisation of our findings for a population undergoing multiple surgeries. Another limitation is that only a very specific population was evaluated, which may not be representative of all elderly subjects submitted to multiple surgeries. Nevertheless, by selecting patients with a consistent clinical history, the homogeneity on the population was increased, diminishing the probability that the cognitive decline detected was due to other causes.

A preoperative cognitive evaluation is lacking on this study. A baseline change in cognition after surgery will allow to establish more secure connection between cognitive decline and surgical stress.[6,7]

Identifying risk predictors before surgery, such as infection or previous multiple surgeries has the advantage of generating more informed future clinical decisions. Detection of cognitive decline may help preventing clinical deterioration as patients are prone to experience difficulties in decision making, regarding further diagnosis and treatment or in following therapeutic instructions, increasing the risk of further physical deterioration.[2]

In conclusion, significantly low cognitive performance on the MoCA test were found on an elderly population submitted to multiple surgeries and periprosthetic infection. Improving the detection of population at risk for cognitive decline is essential for further research designs. A better understanding of the pathophysiology and risk factors is necessary for enhancing current perspectives of treatment and prevention.

Agradecimentos

Ao meu orientador, Professor Doutor Miguel Castelo-Branco, pela orientação científica e incentivo ao espírito crítico e à elaboração do estudo.

Ao Doutor Francisco Oliveira, pela paciência e orientação nas diferentes fases do estudo e à Doutora Nádia Canário, pelo apoio e colaboração no estudo, dentro e fora de horas.

A todo o departamento de Ortopedia, por ter sido tão bem-recebida e com especial apreço ao Doutor Alfredo Figueiredo, pela incansável disponibilidade e cooperação na avaliação dos doentes.

Um agradecimento muito especial aos participantes pela participação no projeto.

Por último, um obrigado à minha família e aos amigos, sem os quais nada faria sentido.

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