

THE USEFULNESS OF GRONINGEN FRAILITY INDICATOR IN THE UROLOGIC PATIENTS AGED OVER 60 YEARS OLD

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THE USEFULNESS OF GRONINGEN FRAILITY INDICATOR IN THE UROLOGIC PATIENTS AGED OVER 60 YEARS OLD (Abstract): The presence of frailty in an older patient influences his mental status, physical status, his response in stress conditions, including surgery and choosing the proper treatment. The surgical community has recently adopted frailty evaluation as an instrument to estimate the post-surgical risk. Our objective is to evaluate the usefulness of frailty evaluation in the urological patient in terms of post-surgical evolution and post-surgical complications. **Material and methods:** This is a prospective study which included 600 consecutive patients aged 60 and over admitted in Urological Clinic in one year. Demographic data and data regarding comorbidities, urological intervention, hospitalization days and complications were collected. Using Groningen Frailty Index (GFI) patients were divided into two groups: non-frail (GFI 0-4) and frail (GFI 5-15). **Results:** 343 patients with a mean age of 70.24 years were in non-frail group and 257 patients with a mean age of 73.28 years in frail group. Cardiovascular comorbidities predominated in both groups 82.02% (281 patients) in the “non-frail” group and in 84.27% (217 patients) in the “frail” group ($p = 0.4833$). Surgical intervention were performed on 80.39% (276 patients) in the “non-frail” group and on 75.40% (194 patients) in the “frail” group. The rate of post-surgical complications was with 13.7% (34 patients) higher in the frail group ($p = 0.00053$). Frailty is correlated with age ($r = 0.252$, $p < 0.0001$), neurological comorbidities ($r = 0.171$, $p < 0.0001$) and non-urological malignancies ($r = 0.096$, $p = 0.018$). **Conclusions:** GFI can be a useful tool in the post-surgical evaluation of the elder patients’ evolution. **Keywords:** FRAILITY, UROLOGICAL OLDER PATIENTS, COMPLICATIONS.

Once with the increase of the average life expectancy, the addressability for conditions that require urological surgery also increases, while an accurate estimation of the surgical risk becomes even more necessary. Elder patients have an increased risk of developing post-surgical complications and major urological inter-

ventions (radical nephrectomy, radical cystectomy, prostatectomy etc.) add even more risks. In case these complications occur, they can lead to a multitude of events resulting in a low-quality life, possible loss of independence, high costs of medical care and increased mortality (1). When dealing with an elder patient, taking

the right decision regarding the surgery, becomes difficult and even a real challenge, due to the complexity of elements which play a role in a healthy condition and the lack of instruments which may appreciate/predict the surgical risk (1).

Elements predicting the post-surgical complications commonly used have substantial limitations-most of them are based on a single organ system or are subjective and do not evaluate the physiological supply of the patients (e.g. Lee and Eagle criteria appreciate only the heart function, while the well-known ASA indicator is determined by a subjective estimation of the level of damage in the organ systems and probability of survival) (1, 2). Hence, some elder patients could be subjected to surgical procedures with an unacceptable high risk of post-surgical complications (2, 3). Both the patient and his relatives must be correctly informed about the surgical risk (4, 5) and the possible short-term and long-term complications which may arise, and for now, the urologist cannot offer answers to match the expectations. For the first time in literature, we have tried to evaluate the usefulness of frailty evaluation in the urological patient by using the Groningen frailty indicator in the view of the post-surgical evolution.

The geriatric community acknowledged and developed the concept of “frailty” for a more accurate objectification of the patients’ condition, defined as an individual syndrome of physiological supply reduction, which restricts the ability of a patient to respond to stress factors and exposes the patients to adverse reactions/results (1, 6).

The surgical community has recently adopted frailty evaluation as an instrument to estimate the post-surgical risk (2).

The aim of this study is to establish the

role that the frailty of the patient-evaluated with the help of the Groningen frailty indicator-can play in appreciating the risks and complications in the pre- and post-surgery periods. It is the first of several studies that explores frailty and its impact on the post-surgical evolution, including oral and maxillofacial surgery, and orthopedic surgery.

The assumed objectives of this study, were: to detect the patients with increased frailty, who could not be identified through other methods (clinical/non-clinical), with the help of the Groningen frailty indicator; establishing the implications of the frailty rate in choosing the urological therapeutic strategy (conservatory/surgical-endoscopic/opened); evaluating the influence of the frailty rate over the surgical risk and subsequent complications.

MATERIAL AND METHODS

In the ongoing study, we have evaluated patients aged over 60 years, hospitalized in the Urology clinic of the “Dr. C. I. Parhon” Hospital in the last 18 months, by filling in a *Groningen Frailty Indicator* (GFI) form at admission. Based on the obtained indicator, these were divided into 2 study groups: 0-4 GFI indicator (considered as “non-frail”) and 5-15 GFI indicator (considered as “frail”). The 2 groups were evaluated comparatively in terms of cardiovascular, neurological, pulmonary, metabolic conditions, but also in what the number of hospitalization days and post-surgical complications are concerned.

600 patients aged over 60 years were included in the study. They were hospitalized in the Urology clinic of the “Dr. C.I. Parhon” Hospital between the 1st June 2017 and 1st May 2018. The GFI form was filled in for all the patients, after the informed consent was obtained.

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The Groningen Indicator is a tool of screening the level of frailty in patients and includes 15 questions. The questionnaire is divided into 4 geriatric fields: physical function (mobility, daily activities, sight, hearing, weight loss); cognitive function; social function (solitude); psychological function (anxiety, depression).

The categories of answers are positively or negatively formulated variables (0 or 1 point). The indicator may vary from 0 to 15 points. High indicators reveal high levels of frailty: patients with a GFI \geq 4, were considered as frail. The patients were also asked about the following socio-demographical data: age, gender, civil status, origin environment (urban/rural). The studied age groups were young elders (60-74 years old), adult elders (75-84 years old) and old elders (\geq 85 years old).

Data concerning the following were collected: patient comorbidities (cardiac, neurological, respiratory, metabolic pathologies or other malignancies), urological pathology-malignant, lithiasis. Infectious (urosepsis, orchiepididymitis, prostatitis), others (periurethral adenoma, hydrocele, trauma); surgical intervention (invasive/opened or minimally invasive/endoscopic); number of hospitalization days; with/ without post-surgical complications.

The statistical analysis was carried out by using *t-Student* and *Chi-Square* and the statistical significance was defined for $p \leq 0.05$.

RESULTS

Between the 1st June 2017 and 1st May 2018, 600 patients hospitalized in the Urology clinic Iasi for a surgical intervention, have filled in the Groningen questionnaire. The patients were aged between 60 and 95 years. Out of these, 33% were women (198

patients) and 67% were men (402 patients). After filling in the questionnaire, 343 patients with a mean age of 70.24 years fell into the 1st study group ("non-frail"), while 257 patients with a mean age of 73.28 years ($p = 0.00001$), fell into the study group of "frail" patients. The origin environment was not significant for the statistics ($p = 0.1034$): in the "non-frail" group, 50.14% (172 patients) were from urban environment and 49.86% (171 patients) from rural environment, while in the "frail" group, 44.35% (114 patients) were from urban environment and 55.65% (143 patients) from rural environment.

Among the associated comorbidities, cardiovascular disease had the highest incidence in both study groups, present in 82.02% (281 patients) of the "non-frail" patients and in 84.27% (217 patients) of the "frail" patients, without being relevant in the statistics between the two categories ($p = 0.4833$).

Neurological conditions (19.35%, $p = 0.000315$), metabolic conditions (33.87%, $p = 0.0196$) and post-surgical complications (13.70%, $p = 0.00053$) had a higher incidence in the "frail" study group, with an impact on the number of hospitalization days, representing an average of 5.97 days (tab. I).

Surgical intervention was carried out on 80.39% (276 patients) of the "non-frail" group and on 75.40% (194 patients) of the "frail" group. In the latter one, the rate of post-surgical complications was with 13.7% (34 patients) higher compared to the "non-frail" group of patients ($p = 0.00053$) (tab. II).

There are no substantial statistical differences regarding the gender of the study group ($p = 0.81$), yet a predominance of male patients can be noticed (tab. III).

TABLE I
Characteristics of the study group according to frailty status

		Non-frail	Frail	p
Number of patients included		343	257	
Age		60-88	60-95	0.000010
Mean age		70.24	73.28	
Gender		F- 95 (26.14%) M-248 (73.86%)	F- 103 (32.66%) M- 154 (67.34%)	0.092954
Environment		U- 172 (50.14%) R-171 (49.86%)	U- 114 (44.35%) R- 143 (55.65%)	0.103400
Comorbidities	Cardiovascular	281 (82.02%)	217 (84.27%)	0.483300
	Neurological	30 (8.82%)	50 (19.35%)	0.000315
	Pulmonary	44 (12.74%)	35 (13.70%)	0.7385
	Metabolic	85 (24.83%)	87 (33.87%)	0.0196
	Other malignancies	25 (7.18%)	32 (12.5%)	0.0345
Urological pathology				0.202
Neoplasia		127	98	
Lithiasis		80	49	
Infectious		41	41	
Others		95	69	
Operated		276 (80.39%)	194 (75.40%)	0.15750
Days of hospitalization		1-64 (5.85)	1-33 (5.97)	0.38400
Complications		16 (5.22%)	34(13.70%)	0.00053

F-female, M-male, U- urban area, R-rural area.

There is a significant statistical difference between the origin environment of the adult elder patients and young elders or old elder ones 116 (60.4%) vs. 178 (46.4%) and 12 (50%). Taking comorbidities into consideration, the cardiovascular ones are more frequently encountered in the age group of 75-84 years old (90.1%), compared to the age group of 60-74 years old (79.4%) and the group over 85 years old (83.3%), the difference proving significant in terms of statistics ($p = 0.0006$). The neurological pathology is encountered on a larger scale in the study group of old elders (37.5%) than in the group of young elders (12.2%) and adult elders (14.1%), the difference between these also proving statistically relevant ($p = 0.002$). There are no statistically significant differences in what the pulmonary or neo-

plasia pathologies are concerned, other than the urological one ($p = 0.299$).

When analyzing the urological pathology according to age groups, statistically significant differences ($p = 0.001$) can be noticed, with a prevalence of the neoplasia pathology, regardless of age, especially in the old elders group (48.5% vs. 41.7% and 33.3%). Urological infectious pathology prevails in the age group ≥ 85 years old (25% vs. 12.8% and 11.5%), while the lithiasis pathology prevails in young elders (24%) compared to adult elders (17.2%) and old elders (4.2%).

Surgical intervention was carried out with no difference in age in the studied group ($p = 0.219$), encountered in approximately 308 (80.2%) patients aged < 75 years old, in 142 (74%) patients aged be-

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tween 75 and 84 years old and in 18 (75%) patients aged over 85 years old. The emergence of complications was similar between the studied groups (35 (9.1%) vs. 20 (10.4%) vs. 5 (20.8%), $p = 0.183$).

Elders ≥ 85 years old are frailer compared to the ones from other age groups, so that the GFI has an average of 7 (8-3) in old elders, vs. 3 (5-1) in young elders, vs. 4 (6-2) in adult elders $p < 0.0001$ (tab. II).

TABLE II
Characteristics of the study group according to age

		Age < 75 years old No.=384	Age 75-84 years old No.=192	Age ≥ 85 years old No.=24	p
Gender	Male	264 (68.8%)	146 (76%)	20 (83.3%)	0.81
	Female	120 (31.3%)	46 (24%)	4 (16.7%)	
Rural		178 (46.4%)	116 (60.4%)	12 (50%)	0.006
Comorbidities	Cardiovascular	305 (79.4%)	173 (90.1%)	20 (83.3%)	0.006
	Neurological	47 (12.2%)	27 (14.1%)	9 (37.5%)	0.002
	Pulmonary	46 (12%)	29 (15.1%)	3 (12.5%)	0.575
	Malignancies	37 (9.6%)	18 (9.4%)	0	0.299
Urological pathology	Neoplasia	160 (41.7%)	64 (33.3%)	11 (48.5%)	0.001
	Lithiasis	92 (24%)	33 (17.2%)	1 (4.2%)	
	Infectious	49 (12.8%)	22 (11.5%)	6 (25%)	
	Others	83 (21.6%)	73 (38%)	6 (25%)	
Operated		308 (80.2%)	142 (74%)	18 (75%)	0.219
Days of hospitalization		5.90 \pm 4.90	5.81 \pm 3.92	5.75 \pm 3.43	0.967
Complications		35 (9.1%)	20 (10.4%)	5 (20.8%)	0.183
GFI		3 (5-1)	4 (6-2)	7 (8-3)	<0.0001

Table note: GFI-Groningen frailty index

TABLE III
Correlations of frailty with the studied parameters

		r	p
Age		0.252	<0.0001
Gender		-0.067	0.100
Rural		-0.862	0.045
Comorbidities	Cardiovascular	0.006	0.855
	Neurological	0.171	0.000025
	Pulmonary	0.012	0.763
	Malignancies	0.096	0.018
Urological pathology	Neoplasia	-0.002	0.969
	Lithiasis		
	Infectious		
	Others		
Operated		0.055	0.180
Days of hospitalization		0.036	0.379
Complications		-0.173	0.00002

The frailty in the older patients hospitalized for urological conditions, is correlated to age ($r = 0.252$, $p < 0.0001$), presence of neurological disease ($r = 0.171$, $p < 0.0001$) and non-urological malignancies ($r = 0.096$, $p = 0.018$). Frailty is also correlated to the rural origin environment ($r = 0.862$, $p = 0.045$), GFI proving to be higher in those. The presence of complications was associated to frailty in the elders from the studied group ($p < 0.0001$). The days of hospitalization ($p = 0.379$), type of urological pathology ($p = 0.969$), presence of cardiovascular ($p = 0.855$), pulmonary ($p = 0.763$) conditions and days of hospitalization ($p = 0.379$) were not associated to frailty (tab. III).

DISCUSSION

There are numerous studies searching for the right tools to quantify the actual health condition regardless of age (7). Among these, the Groningen indicator seems to be a useful element in establishing the frailty. Meulendijks *et al.* believe that "frailty" with a reduced level of psychological supply is caused by the accumulation of multiple deficits of the organs, resulting in an extremely low endurance to stress (9). In a study carried out on 1549 patients, Irene Drubbel *et al.* certify the usefulness of the Groningen questionnaire, compared to the Frailty Index (FI).

Currently, approximately half of the surgical interventions from USA are carried on patients older than 65 years old. Based on recent population projections, it is estimated that the average workload of surgeons shall increase from 14% up to 47% between 2000 and 2020, because of the old patients. (1). There is no doubt concerning the fact that these patients require a specific approach and the presence

of frailty must be taken into consideration in the treatment scheme (8). Due to similar trends in our population, we perform this study to identify particularities and significance of frailty. In our study group the frailty population as older than the non-frail group with no significant differences between men and women. The prevalence of frailty of 42,83% in our group was higher comparing with other data (21,8% in a study perform by Moro *et al.*) despite the fact that our group included patients over 60 years, compared with 70 years in the other study (29). This may be a characteristic of our population, or an indicator for "the biological age" of our study population considering the high prevalence of comorbidities, over 80 % had concomitant cardiovascular comorbidities, but also metabolic and neurological ones.

Once the patient was identified as frail, the physician can consider the risks and benefits of a potential surgical intervention. In the post-surgery period, it is possible to reduce the risk of complications in the frail ones, through a more careful monitoring, a better hydration, nutrition and mobilization. (1) In a study carried on 594 patients aged ≥ 65 years old, who needed an elective surgical intervention, Martin A. *et al* shows that frailty is an independent factor which predicts post-surgical complications and the number of hospitalization days. (1) These data comply with the results of our study, where frail elders had greater complications compared to the non-frail since the frailty indicator is associated with the emergence of complications. This can be the context for body homeostasis condition, affecting the adaptive ability and association of sarcopenia. All the things mentioned above are body modifications in the context of the emergence of a frail state

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and negatively influence the response of the body to stress, causing an increased risk of morbi-mortality (14, 15). Post-surgery complications are frequent in frail-group, but also depends of patients age. In our study, the very old group, aged over 85 years, 20.8% had complications, compared with those below 75 years of age; and the older the patient, the higher the GFI. Similar findings were described in a previous study which included 95,108 urologic cases representing 21 urologic procedures. They found that frailty is strongly associated with both major and minor complications among patients undergoing urologic surgery. Moreover, frailty had a significant association with complications for most urologic procedures examined. (30) Louis M Revenig et. al carries out a similar study on 80 patients and finds the same negative impact on the post-surgical evolution in patients categorized as "frail" after filling in the questionnaire, compared to those considered as "non-frail" and even reported an increased incidence of post-surgical complications in case of open, extensive, elaborate surgical interventions, compared to the endoscopic, urological and minimally invasive ones (6). Further data emphasize the fact that the presence of frailty is a strong predictor of high-grade post-operative complications and mortality following radical cystectomy in bladder cancer patients. Thus, frailty has the potential to be a very clinical aspect for risk stratification and perioperative counseling of bladder cancer patients (31).

Frailty and the emergence of post-surgical complications bring about the increase of the hospitalization period and mortality (16, 17, 18). In our study group, the hospitalization period was similar in frail and non-frail patients and also with no

differences regarding patients age (considering the three groups). The explanation results from the multi-disciplinary collaboration in the hospital, which facilitated the post-surgical identification of frail elder patients. Hence, corrective actions could be carried out and a customized tracking of these could be established, while post-surgery, patients were transferred in the Geriatric Clinic, if the case.

The geriatrist R. E. Hubbard and anesthesiologist D. A. Story defined frailty and its quantification as "an elephant in the operating room: easy to spot, yet often ignored". They define frailty as that increased vulnerability of the geriatric patient to intra and post-surgical stress, seen as the mirror of the normal process of aging, but which manifests differently; although there are validated algorithms and questionnaires, it is difficult to quantify the elements leading to an increased risk up to being unacceptable, when talking about an elder patient going into the operating room (12, 32).

Only one study, carried out in Romania by Marinela Olariu (13) validates the Groningen indicator as useful in evaluating elder patients' frailty and finds a much greater prevalence in Romanian patients compared to the Dutch ones. Thus, this study provides significant data regarding frailty in elders hospitalized for urological conditions. The great number of patients included in the study increase the importance of the results, since they can be extrapolated to other similar populations. Also, this study is one of the few studies which stress out the necessity of post-surgical evaluation of frailty in the urological patient, even in the surgical one, and of collaborating with the geriatric team in order to reduce the complications and hos-

pitalization period.

There are several limitations to our study including a limited follow-up period, leading to an underestimation of complications. The anesthesia type is not recorded, and the literature data described a relationship between depth of anesthesia and impaired postoperative also suggested a more pronounced impact on the elderly and especially in pre-frail or frail patients (33). Also, data about the cognitive status, sarcopenia and other geriatric syndromes is lacking (34, 35). These data emphasizes the need for further studies.

CONCLUSIONS

In order to make a correct decision regarding the surgical treatment, it is useful to establish whether the patient is frail or

not, by taking into consideration the tight connection between frailty and the increased risk of developing post-surgical complications.

A large part of the urological patients is over 60 years old and anticipating the emergence of post-surgical complications within the context of their age, surgical intervention and comorbidities, is still a challenge. The experience accumulated from those 600 patients indicates the fact that the Groningen indicator can be a useful tool in the post-surgical evaluation of the elder patients' evolution.

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NEWS

EVALUATION OF THE EFFECTS OF BIOCOMPATIBLE MATERIALS ON CELL DEVELOPMENT ON PULP STEM CELLS IN DIRECT PULP CAPPING

A group of researchers have studied the effects of widely used biomaterials in direct capping, using the in vitro method on pulp stem cells. The osteogenetic, odontogenetic and angiogenetic effects of ProRoot MTA (Dentsply Tulsa Dental Specialties, Johnson City, TN, USA), Dycal (DENTSPLY Caulk, USA), Biodentine (Septodont, USA) or Emdogain Gel 30 mg/ml (BIORA AB/Straumann, Switzerland) were studied on stem cell cultures. The analyzes of the genetic markers were performed during a time span of 7 to 14 days following the beginning of the experiment and the goal was to preserve the pulp vitality in the cases group compared to the control group. Statistical analysis was done by one-way ANOVA. The study revealed that Emdogain has a lower cytotoxicity than the other materials. In the case of osteogenesis and odontogenesis it was concluded that all 4 materials stimulate these processes, but Dycal exhibited lower results in angiogenesis, compared to the other materials. Therefore, Emdogain can be a successful material in direct capping due to its biological properties, particularly involved in pulp regeneration (Abdel-Rahman Y., Ramy E., Mohiuddin M. T., Faisal A. Al-Alla, Majed A., Mazen A. A, Shahid S. S. Effects of mineral trioxide aggregate, calcium hydroxide, biodentine and Emdogain on osteogenesis, Odontogenesis, angiogenesis and cell viability of dental pulp stem cells. *BMC Oral Health* 2019; 19: 133).