Oncogeriatric Assessment: A Key Step in the Preoperative Workup. Case Report of a Duodenopancreatectomy in an 80-Year-Old Patient

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Abstract

Background: Pancreatic cancer is the 12th most common malignancy worldwide and the 7th leading cause of cancer mortality. Its incidence is increasing in older people, who are particularly characterized by high phenotypic variability in terms of comorbidity, dependence, nutritional and cognitive impairment, each of those being able to interact with the results of reference therapies. Aging is a heterogeneous process that cannot be understood simply by chronological age and must take into account all of these factors. The Comprehensive Geriatric Assessment (CGA) must therefore play an important role in therapeutic reflection to avoid over- or under-treatment in this population. This assessment identifies previously unknown geriatric syndromes in nearly 50% of cases, but also leads to specific interventions in a quarter of cases, and modifies the choice of oncological treatment in 20% to 25% of cases in order to find the best association between quality of life and quantity of life. This reflection on the best therapies and their implementation must be established with the patient himself from the beginning of the treatment.

Case Report: Mrs. M is 80 years old, independent and in good condition. She presented with jaundice without fever, which led to discover an adenocarcinoma of the head of the pancreas by Magnetic Resonance Imaging (MRI), and echo-endoscopy, without any secondary lesions on imaging. Following the patient's wishes and the oncogeriatric opinion, it was decided to perform a cephalic duodenopancreatectomy. The patient recovered progressively and it was decided to start adjuvant chemotherapy for a pT3N1b stage. After a stay in follow-up care and rehabilitation allowing a resumption of her autonomy, a good nutritional status, and the setting up of a care network at home, the patient returned home.

Conclusion: Despite its aggressive nature and an often more frailty phenotype of older people, treatment options in pancreatic cancer are not absent for this population. Just as the evaluation of the cancer itself requires TNM staging, the evaluation of the elderly cancer patient must include an oncogeriatric evaluation to provide the best management according to the patient's wishes and the treatment options available. This evaluation can lead to a pre-habilitation program to give the patient all chances to benefit from the best possible results.

Keywords: Cancer pancreas; Screening; Frailty; Therapeutic decision; Surgery

Background

Median age at diagnosis of pancreatic cancer is 69 years for men and 73 years for women. Therefore, pancreatic cancer is particularly prevalent in the elderly population [1]. Incidence and mortality of pancreatic cancer are highest in countries with a very high human development index, which are also countries with a higher life expectancy. Occurrence of clinical signs in pancreatic cancer often marks a turning point in the history of the disease and is often a sign of extensive lesion involvement. Pancreatic cancer remains, despite many advances in treatment, an extremely aggressive disease with a low survival rate [2].

Pancreatic cancer faces two major problems related both to its aggressiveness and to the population affected, which is phenotypically very diverse. Elderly patients are not all equal regarding the disease and they present in a very heterogeneous way, numerous comorbidities and geriatric syndromes (under nutrition, dependence, neurocognitive disorders, functional alteration, etc.) likely to be associated with poor results of anti-cancer treatments [3,4]. Management of this disease in an elderly population that is particularly heterogeneous requires serious consideration and cannot be based simply on age [5]. What treatment should be proposed to this population, which is also less represented in clinical trials and more at risk of side effects? [6,7] Oncogeriatric assessment must therefore play a full role in the therapeutic decision and guide multidisciplinary management to improve the quantity and quality of life [8,9].

Case Presentation

Mrs. M is 80 years old, widowed and lives alone. She has two sons, one of whom lives near her home. She is perfectly autonomous for all activities of daily living. Her history includes mainly cardiovascular diseases with a narrow aortic stenosis requiring a bioprosthesis two years ago, an atrial fibrillation and a stenosis of the anterior interventricular artery <30%. Her treatments include: Apixaban, sotalol, furosemide, ramipril, esomeprazole.

Mrs. M consulted the emergency room for jaundice without fever, which led to discover a 30 mm cephalic-isthmic pancreatic tissue lesion suggestive of cancer by an MRI and then an echo-endoscopy. No vascular invasion was identified on imaging. During the echo-endoscopy, a metallic prosthesis was placed. The extension workup did not find any secondary lesion. The biopsies taken during the echo-endoscopy came back in favor of a differentiated adenocarcinoma at the cephalic level and of the ampulla of Vater on Intraductal Papillary Mucinous Tumors of the Pancreas (IPMTP).

Before any decision was made to proceed with surgery and before Tumor Board Meeting (TMB), Mrs. M underwent an oncogeriatric assessment to detect any geriatric syndromes that might compromise this optimal management. This evaluation revealed that her functional autonomy was perfectly preserved with an Activities of Daily Living (ADL) score of 6/6 and Instrumental Activities of Daily Living (IADL) score of 8/8, the absence of falls and regular physical activity. She also had under nutrition with an albumin level of 31 g/L and a Body Mass Index (BMI) of 18.5 kg/m², the absence of dysthymia and cognitive complaints with a Mini Mental State Examination (MMSE) screening score of 29/30. All the criteria evaluated during this comprehensive geriatric assessment were in favor of surgical and medication management according to the guidelines. Mrs. M

Table 1: The G8 screening tool [17,18].

Items	Score
1: Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing difficulties?	0=severe decrease in food intake
	1=moderate decrease in food intake
	2=no decrease in food intake
2: Weight loss during the last 3 months	0=weight loss greater than 3 kg
	1=does not know
	2=weight loss between 1 and 3 kg
	3=no weight loss
3: Mobility	0=bed or chair bound
	1=able to get out of bed/chair but does not go out
	2=goes out
4: Neuropsychological problems	0=severe dementia or depression
	1=mild dementia
	2=no psychological problems
5: BMI=weight in kg/(height in m)^2	0=BMI less than 19
	1=BMI 19 to less than 21
	2=BMI 21 to less than 23
	3=BMI 23 or greater
6: Takes more than 3 prescription drugs per day	0=yes
	1=no
7: In comparison with other people of the same age, how does the patient consider his/her health status?	0=not as good
	0.5=does not know
	1=as good
	2=better
8: Age	0=>85 years
	1=80–85 years
	2=<80 years
Total Score	0-17

A score ≤ 14/17 indicates geriatric frailty or vulnerability requiring a CGA
BMI: Body Mass Index

Table 2: The modified G8 [19].

Items	Score
1: Has food intake declined over the past 3 months due to loss of appetite, digestive problems, chewing or swallowing diffculties?	0=severe decrease in food intake
	1=moderate decrease in food intake
	2=no decrease in food intake
2: Weight loss during the last 3 months	0=weight loss greater than 3 kg
	1=does not know
	2=weight loss between 1 and 3 kg
	3=no weight loss
3: Mobility	0=bed or chair bound
	1=able to get out of bed/chair but does not go out
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4: Neuropsychological problems	0=severe dementia or depression
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5: BMI=weight in kg/(height in m)^2	0=BMI less than 19
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6: Takes more than 3 prescription drugs per day	0=yes
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	0.5=does not know
	1=as good
	2=better
8: Age	0=>85 years
	1=80–85 years
	2=<80 years
Total Score	**0-17**

A score ≥ 6 on the modified G8 indicates the presence of a frailty that should lead to the performance of a CGA

underwent cephalic duodenopancreatectomy with pancreatogastric anastomosis. Three of the 24 lymph nodes removed during the surgery came back metastasized by the adenocarcinoma, thus classifying the patient's cancer as pT3N1b. There wasn't indication of neoadjuvant chemotherapy.

Postoperatively, the patient presented a super infection of an abscess found in the surgical blade associated with an intraperitoneal effusion of medium abundance having required an antibiotic therapy with Tazocillin for 5 days. Eighteen days after the operation, the patient presented a hemorrhagic shock with blackish vomiting in a context of curatively anticoagulated atrial fibrillation. Upper gastrointestinal endoscopy revealed a large clot in the gastric body, but no fresh blood. A clip was then placed on an 8mm platelet nail found on the posterior aspect of the subcardial region and hemospray was applied on 15 mm superficial ulceration. After stabilization, the patient was transferred to a follow-up care and rehabilitation unit. After discussion in a Tumor Board Meeting (TBM), and in view of the patient's fragile general condition and nutritional status, it was suggested that the patient undergo consolidation of these elements before starting adjuvant chemotherapy with Capecitabine. Mrs. M was able to return home and the chemotherapy sessions were started with good tolerance.

Discussion

Pancreatic cancer in people over 80

Pancreatic cancer is one of the cancers that cause more geriatric complications postoperatively, which may in turn lead to a greater risk of developing other complications, increase hospital mortality or lead to greater recourse to rehabilitation care, thus leading to a longer length of stay and higher costs associated with care [3]. Results after pancreatic resection in octogenarians are still controversial. In a recent review of the literature, aimed at analyzing existing data on early postoperative and long-term outcomes after pancreatic resection in patients aged 80 years and older, almost all authors affirmed that pancreatectomy can be performed safely in the elderly. Despite morbidity and overall mortality rates of 34.9% and 13.2% respectively, with mean lengths of stay of 18 days after surgery, long-term survival was not significantly different in patients over 80 years of age with an overall survival of 17.6 months [10,11].

Therefore, age cannot be the only limiting factor in the decision of surgical management of pancreatic head cancer [12]. Considering that the mortality rate and perioperative morbidity remain high in octogenarians, and the significant phenotypic variability of these patients in terms of geriatric comorbidities, the selection of these

Table 3: VES-13 screening scale [20].

Items	Score
Age:	
- 75-84 years old	1
- ≥ 85 years old	3
In general, compared to other people your age, would you say that your health is:	
- Excellent, very good or good	0
- Fair or poor	1
Because of your health or physical condition, do you need help for:	
- Shopping for personal items?	1
- Managing money?	1
- Walking across the room (use of a cane or walker is okay)?	1
- Doing light housework?	1
- Bathing or showering?	
Do you have difficulty with the following activities:	
- Stopping, crouching, or kneeling?	1
- Lifting or carrying objects as heavy as 5 kg?	1
- Reaching or extending arms above shoulder level?	1
- Heavy housework such as scrubbing floors or washing windows?	1
- Writing or handling and grasping small objects?	1
- Walking 500 m?	

A score ≥ 3 on the VES-13 indicates the presence of an increased risk of death and functional impairment
- Risk of functional decline: score 1-2: 11.8%; score ≥ 3: 49.8
- Risk of death: score 1-3: 14.8%; score ≥ 4: 54.9

Table 4: Components of the DELPHI score [34].

Items	Points
Age (years)	
- 60-69	0
- 70-79	1
- ≥80	2
Low physical activity	
- Self-sufficient	0
- Need assistance	2
Alcoholism	
- No	0
- Yes	1
Hearing impairment	
- No	0
- Yes	1
History of delirium	
- No	0
- Yes	2
Emergency surgery	
- No	0
- Yes	1
Upen surgery	
- No	0
- Yes	2
Intensive care unit admission	
- No	0
- Yes	3
C-reactive protein rate (mg/dL)	
- < 10	0
- ≥ 10	1
Score	**15**

≥ 7/15 score predicts an 81% risk of developing perioperative confusion

patients must remain an important step [13]. In studies on the surgical treatment of pancreatic cancer in the elderly, quality of life has been less evaluated, although it plays an important role in the therapeutic decision in this population. The lack of space in rehabilitation services may also affect postoperative recovery and thus counterbalance the benefits of surgery. Keys of success for this type of surgery in elderly patients require a good selection of patients, a geriatric evaluation with a multidisciplinary approach, trained surgical centers and a good partnership with rehabilitation centers for the implementation of a post-operative rehabilitation program [3].

Comprehensive geriatric assessment

A consensus of the International Society of Geriatric Oncology (SIOG) and geriatric oncology experts recommends a CGA for elderly (>75 years) cancer patients [8,9,14]. Thus, screening frailer patients with geriatric syndromes or those likely to develop them during their oncological disease helps to identify patients eligible for index treatment and to manage a number of factors that may interfere with their success. In a 2016 study initiated by SIOG, 80% of surgeons reported that they were not limited by age in proposing surgery for cancer management. To assess fitness for surgery, they said they primarily used the American Society of Anesthesiology (ASA) score, the Eastern Cooperative Oncology Group (ECOG) Performance Status (PS), nutritional status, the Physiological and Operative Severity Score for the enumeration of Mortality and morbidity (POSSIUM) or the Mini Mental State Examination (MMSE) [15].

In order to perform a CGA in the elderly population to guide the treatment decision, geriatricians established a number of recommendations [8,9,14,16]. A CGA requires significant time and resources and is not achievable for all patients. Screening tools have therefore been developed and some of them allow the physician/surgeon or nurse to identify patients who should require a CGA. These tools are simple, quick and highly sensitive to avoid misidentifying fragile patients. Two scores exist in oncogeriatrics to search for this frailty and to guide towards a more in-depth geriatric assessment. These are the G8, which has been specifically validated for elderly patients in oncogeriatrics, and the Vulnerable Elders Survey-13 (VES-13) 17181920 (Tables 1-3).

After identifying frail elderly patients by screening tools, CGA will allow to assess the patient's functional reserve and life expectancy, to rank the importance of the various comorbidities from which patients suffer, but also to recognize and manage a certain number of geriatric syndromes which may alter the patient's quality of life and interact with the tolerance of oncological treatments. The CGA therefore explores specific geriatric domains: Comorbidities, functional autonomy, risk of falls, cognitive and psychic disorders, nutritional status, sensory and continence disorders, and the social environment. Some teams will also assess the risk of delirium, which is a problem frequently encountered in elderly patients and which can lead to complications and compromise oncological treatment, whether it be drug or surgical. For each domain, several tools are available, but there is no consensus on which tool to use and on the

optimal thresholds or cut-off scores [14-21].

To assess the burden of comorbidities, two scales exist: The Charlson score, and the Cumulative Illness Rating Scale - Geriatric (CIRS-G) [22,23]. Although an age-adapted version of the Charlson has been developed, it nevertheless assesses certain comorbidities that are less prevalent in the elderly patient, such as HIV infection, and it does not take into account the presence of under nutrition or hypertension. The CIRS-G scale is more adapted to the geriatric population. Geriatricians recommend the use of the Activities of Daily Living (ADL) and Instrumental Activities of Daily Living (IADL) scales to assess patient's functional autonomy [24,25]. The primary tests used to assess balance and motor performance in elderly patients are the Timed Up and Go test (TUG), monopodal stance for 5 sec, and gait speed [26,27]. The most commonly used tool to screen depressive syndrome is the Geriatric Depression Scale (GDS) in its short 15-item version [28,29]. The mini-GDS, which has only 4 items, offers good sensitivity and specificity compared with the GDS for rapid detection of a depressive syndrome if the score is greater than or equal to 1/4 [30]. Screening for neurocognitive disorders is based on the Mini Mental Status Examination (MMSE) or the Mini-Cog [31-33]. Even if the risk of delirium is not strictly part of the targets of CGA, it is a sign of cognitive fragility and remains interesting to screen for, especially considering that it interferes with the performance of care and the feasibility of certain treatments, in particular surgery. The Delirium Prediction based on Hospital Information (DELPHI) study has developed a score to help medical and surgical teams to predict the onset of delirium in patients with a sensitivity of 80.8% and a specificity of 92.5% [34] (Table 4). Score ≥ 7/15 predicts an 81% risk to develop perioperative delirium. Similarly, the American College of Surgeons designed a tool to provide information on the specific risks for each patient for a given surgical procedure [35]. This tool was created using a database containing 5 million surgical procedures and allows the prediction of a certain number of perioperative complications related to the procedure, but also related to geriatric characteristics collected when the patient is 65 years old or older (cognitive profile of the patient, history of falls, place where the patient lives, etc.). It assesses in particular the risk of delirium. Malnutrition, which is particularly known to have a negative impact on quality of life, reduced immune response, tolerance of anti-cancer treatment and survival, is assessed by the Mini Nutritional Assessment (MNA), albumin measurement (in the absence of inflammatory syndrome) and anthropometric criteria (BMI, brachial circumference, recent weight loss) [36-39].

Assessment of the environment and living conditions is also an important step in the oncogeriatric evaluation. It enables the composition and availability of the family and the resources on which the patient and all the care providers can rely to be assessed.

While recommendations are proposed in more than 95% of cases after a CGA, less than 7 times out of 10 they result in effective interventions [40]. When this evaluation is taken into account, it leads to a change in treatment in 21% of cases (lowered objectives, especially for chemotherapy) and in almost a quarter of cases, the initial care plan is not implemented [41]. Data from CGA with an impact on modification of the treatment plan were mainly under nutrition and impaired functional status. Data on the impact of CGA on survival show that at 6 months, geriatric factors independently associated with cancer death are dependence, impaired mobility, and presence of comorbidities. At 3 years, cognitive impairment, in addition to these different factors, is independently associated

with decreased survival [4,42-45]. To assess longer-term mortality a study evaluated the usefulness of the GRADE score in predicting 5 year mortality in elderly cancer patients. By a combination of simple geriatric parameters such as gait speed and weight loss, and cancer parameters such as cancer site, a preoperative GRADE score ≥ 8 provides a discriminative prognosis on 5 year mortality and may help to select the most appropriate treatment strategy for elderly cancer patients, avoiding under or overtreatment [46].

Elderly cancer patients want to be fully informed about their diagnosis and treatment, and nearly three quarters of these patients want to be involved in decision-making about their care [47]. A true partnership between the medical team and the patient must be established early in the diagnostic process in order to respond to both the patient's wishes and the treatment options. This collaboration is particularly important for the implementation of a presurgical habilitation program, which is sometimes necessary to improve the success of certain surgical procedures and certain anti-cancer drug treatments.

This multimodal pre-habilitation aimed to reinforce the physiological reserve in anticipation of the foreseeable harmful effects of surgery and to facilitate postoperative recovery of functional capacity in the most fragile patients has shown a real benefit as regards functional recovery in the postoperative period, the reduction of postoperative complications and also the reduction of the length of hospital stay [48-51]. This pre-habilitation, which in most cases proposes nutritional and functional management, must be based on the recommendations of the geriatric evaluation and the therapeutic management proposed by TBM, but also on the active participation of the patient. Co-management must therefore be established to promote success and to adapt to the patient's geriatric profile. A study showed that co-management by surgeons and geriatricians during the perioperative period of cancer surgery in elderly patients was associated with a reduction in 90-day mortality and a greater prescription rate of physiotherapy, occupational therapy, speech therapy and nutritional support, which also improved quality of life [52].

Conclusion

Optimal management of pancreatic cancer according to the guidelines of surgical and oncology societies is not incompatible with an age above 80 years. Given the wide range of phenotypic profiles, elderly patients with pancreatic cancer should benefit from a CGA to establish the best management and avoid over- or under-treatment. In the era of molecular biology, genomic studies, advanced surgical techniques and robotics to adapt cancer treatment, CGA remains the first step in personalized medicine for elderly cancer patients. Collaboration between oncology, surgery, organ specialists and geriatrics teams is of major importance for these patients and the generalization of care pathways allowing a multidisciplinary approach is necessary to improve the quality of care and the quality of life of elderly cancer patients.

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