EDITORIAL

Better Visualisation and Proper Preoperative Planning for Surgeons: New Option for Patients

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ABSTRACT

The year 2017 has passed without any major breakthroughs in the field of pancreatic cancer. Despite all attempts to improve the management and long-term outcomes of pancreatic adenocarcinoma, pancreatic cancer still remains a lethal malignancy, and is pushing forward all attempts to diagnose the disease as early as possible. The pancreatic protocol computed tomographic scan with arterial and venous phase enhancement is an accepted diagnostic standard and should be followed in any surgical unit which deals with pancreatic surgery, complemented by magnetic resonance imaging, positron emission tomography or Endoultrasound when indicated. Surgical care has probably arrived at its limits, and other treatment modalities will aid in reaching truly curative long-term outcomes. While the recent development of new agents or combinations may add the hope of improving the disease outcome, a deeper exploration of the molecular, genetic nature and types of immune mechanisms is the direction to follow to reach clinically relevant long-term results.

EDITORIAL

The year 2017 has passed without any major breakthroughs in the field of pancreatic cancer although some innovative strategies in pancreatic surgery and disease recognition have been tested. Despite all attempts to improve the management and long-term outcomes of pancreatic adenocarcinoma, pancreatic cancer still remains a lethal malignancy. The unfortunate evidence that most pancreatic cancer patients are diagnosed with unresectable advanced disease upon arrival to the surgeon and succumb to the disease within one year is pushing forward all attempts to diagnose the disease as early as possible [1, 2, 3]. Early recognition of pancreatic malignancies is the cornerstone of further management of the disease, and imaging plays an important role in it. It is a diagnostic step for preoperative staging and proper preoperative plan of surgical intervention that allows identifying patients who are eligible for curative intent surgical resection. The pancreatic protocol computed tomographic (CT) scan with arterial and venous phase enhancement including submilimiter scans is an accepted diagnostic standard and should be followed in any surgical unit which deals with pancreatic surgery. Currently, positron emission tomography is considered as an adjunct modality to CT in the evaluation of high-risk patients, including borderline resectable disease and markedly elevated CA 19.9, large primary tumours or large regional lymph nodes.

The lymph node 8a has been recognized as a significant prognostic marker for a shorter overall survival. It is even recommended to perform laparoscopic biopsy prior to the definitive surgical intervention for a better preoperative planning of therapeutic strategy. Endoscopic ultrasound (EUS) helps to determine portal vein extension and may confirm the histological diagnosis before neoadjuvant therapy is initiated when occult metastatic disease is identified, including tumours located in the body or tail, large >3 cm [4, 5]. Another advantage of EUS is the lack of need to administer intravenous contrast, which is useful for patients with contraindications to CT or MRI [5]. Complete staging includes the search for distant metastases in the liver and lung, preferably performed by a CT scan and an additional MRI in selected cases, as well as laparoscopic staging when indicated. However, the rational for laparoscopic diagnostics before neoadjuvant therapy to exclude peritoneal involvement is controversial [6].

A personalized approach involving multidisciplinary specialists has improved the treatment of different malignancies, however, not so much in pancreatic cancer. A significant number of chemotherapeutic agents have been tested, especially in cases of advanced disease, without any significant survival benefits, and until recently single-agent gemcitabine, introduced in 1997, was considered the standard. Trials to combine chemotherapy and molecular targeted drugs like erlotinib with gemcitabine have led to some improvement in patient survival, yet the results are far from clinically acceptable [7]. So far, three combination chemotherapies (nab-paclitaxel-gemcitabine, FOLFIRINOX, and PEFG) have shown better results in patients with advanced disease, compared to single-agent

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gemcitabine, while the median survival is 8.6–11 months associated with different degrees of toxicity [7, 8, 9]. The strong agreement is in favour of the use of adjuvant chemotherapy after R0 resection. A pathological diagnosis is considered mandatory before the start of a multimodal treatment, and restaging after preoperative treatment should include CT and/or MRI [6]. Unfortunately, despite advanced surgical techniques and curative-intent surgery including perioperative care, the majority of patients die after surgery due to local recurrence or distant metastatic disease. Unsurprisingly, surgeries performed at high-volume centres have better R0 resection rates and better overall survival rates because of a more appropriate patient selection for curative procedures. Surgical skills and volume are important for an early recovery and a decreasing mortality and morbidity after the procedure. Currently, the state-of-the-art pancreaticodudenal resection involves the so-called mesopancreatic [10] resection margin, including a total mesopancreas excision with even circumferential lymphadenectomy of the SMA to achieve an adequate retropancreatic margin clearance and minimize the likelihood of an R1 resection and local recurrence.

Mesopancreas dissection with central vascular ligation and the superior mesenteric artery (SMA)-first approach represent the cornerstone of the current principles for radical resection of pancreatic head cancer [11]. The abovementioned criteria may be fulfilled by experienced surgeons in a setting with established teamwork principles and a critical assessment of the treatment results. That means certain limits for patients living in areas without highly specialized centres, and for professional surgeons who are faced with insufficient volumes to reach the very top standard of this specific care. This type of surgical care has probably arrived at its limits, and other treatment modalities will aid in reaching truly curative long-term outcomes. Several directions have been explored to recognize the important aspects of the aggressive nature of pancreatic cancer. Pancreatic adenocarcinomas are characterized by genetic heterogeneity which has patient-specific individual patterns and considerable genetic instability. Unknown remains the question whether a number of genetic aberrations occur gradually and simultaneously to carcinogenesis or pancreatic tissue accumulates a number of critical genetic mutations early and the available tissue molecular profiling is very limited [7]. The new and promising direction is the exploration of pancreatic stem cells. According to the current evidence the well-known, inherent chemoresistant nature and metastatic capacity of pancreatic adenocarcinoma might be linked to a subpopulation of highly plastic “stem”-like cells within the tumour with unique properties for a continuous self-renewal and resistance to chemo-therapeutic elimination [12]. One of the major challenges for developing molecularly-targeted therapies is the presence of a few prevalent genetic mutations – KRAS (activating), CDKN2A (encoding p16), TP53 and SMAD4 (inactivating) – without the possibility to correct them with the available pharmacologic treatments and other immune mechanisms [13]. The fundamental aspect of oncology, the induction of the immune response of the host, has been recently studied in a randomised phase II study. The so-called Wilms’ tumor gene 1 vaccine has been combined with gemcitabine and compared to gemcitabine alone [14]. All of the new developments need a more active involvement of clinically-based studies for the exploration of the potential of a maintenance therapy or neoadjuvant treatment in resectable disease or unresectable disease, driven by basic research and translational research.

CONCLUSION

The management of pancreatic cancer has approached its limits considering the potential to treat this aggressive disease surgically. An improved selection of patients based on advanced preoperative visualization and preoperative planning is the only way for the surgeon to go forward; however, it is insufficient for achieving a long-term curative goal. While the recent development of new agents or combinations may add the hope of improving the disease outcome, a deeper exploration of the molecular, genetic nature and types of immune mechanisms is the direction to follow to reach clinically relevant long-term results.

Conflict of Interest

The authors declare no conflict of interest.

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