Editorial Commentary

Shifting paradigm of quality of life after pancreatoduodenectomy for pancreas cancer

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As long-term survival has improved with advancements in pancreatic cancer treatment in the modern era, quality of life (QOL) among pancreatic cancer patients following pancreaticoduodenectomy (PD), i.e., Whipple procedure, warrants understanding and addressing within the medical community. The article by Zhang *et al.*, titled "Quality of Life and Gastrointestinal Symptoms in Long-Term Survivors of Pancreatic Cancer Following Pancreaticoduodenectomy", provides valuable insights into the balance between the overall survival benefits of this complex procedure and patient-reported long-term post-operative effects on patient well-being.

Historically, PD, first described by Alessandro Codivilla in the late 19th century, was a technical marvel and was later refined by Dr. Whipple in the 1930s (1,2). Despite further surgical advancements in the 1950s and 1960s, high morbidity and mortality rates persisted, raising questions about whether the risks of surgery were justified given the generally poor prognosis of pancreatic cancer (3). Even as Cameron *et al.* established new benchmarks for post-Whipple morbidity and mortality in the 2000s, this technical success could not overcome the persistent challenge of low overall survival rates (4). The perception of both pancreatic cancer and the Whipple procedure remained negative for many years, with both the disease and the operation becoming synonymous with a bleak prognosis. However, modern advancements in systemic treatments, imaging modalities, surgical techniques, and post-operative management have led to improvements in mortality and morbidity associated with the Whipple procedure, as well as increased long-term survival among pancreas cancer patients (5). As these outcomes improved, so has our understanding of the physiological and psychological impacts of PD.

The current study by Zhang *et al.* sheds light on key aspects of pancreatic cancer survivorship, particularly QOL and gastrointestinal (GI) symptoms. The study found that long-term survivors of pancreatic cancer who had undergone PD reported a relatively higher QOL compared to the general US population. Although patients experienced chronic post-operative GI symptoms, including pancreatic insufficiency, reflux, and delayed gastric emptying, these symptoms did not significantly affect their overall QOL. Most patients indicated they would undergo surgery again. However, those who reported poorer QOL attributed it to post-operative complications such as pancreatic fistulas, delayed gastric emptying, and incisional hernias. Additionally, patients who expressed reluctance to undergo PD again reported a higher frequency of GI symptoms. These insights should be integrated into the management of recovery and the discussion of long-term lifestyle adjustments. Using the evidence from Zhang and similar studies, surgeons can offer evidence-based reassurance to patients who may be anxious about undergoing this major procedure, while also setting realistic expectations for recovery and the potential long-term

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physiological effects. Overall, long-term cancer survival appears to be the primary driver of QOL, despite ongoing physical challenges.

In our own study, we found that while patients may experience chronic GI issues following surgery, the overall impact on QOL is more significantly influenced by mental well-being and financial factors than by the physiological consequences of PD (6). Furthermore, there were notable differences between patients who underwent PD for malignant versus benign conditions. Patients treated for malignancy reported a significantly worse QOL, citing psychological and socioeconomic challenges related to pancreatic cancer, including feelings of diminished utility, hopelessness, loss of control, uncertainty about the future, dissatisfaction with physical appearance, memory issues, fear of relapse, and financial strain. In contrast, physical health did not have a significant association with QOL, regardless of whether the pathology was benign or malignant. These findings highlight a concern for the undertreatment of depression in patients with pancreatic cancer. Large healthcare systems must better address this gap by providing comprehensive support and counseling, even for patients who have undergone curative surgery, as non-surgical factors tend to have a more profound impact on QOL than the physiological effects of the surgery itself.

While the management of GI issues related to PD, such as malabsorption, diarrhea, and weight loss, is essential, multiple studies emphasize the significant psychological and socioeconomic challenges faced by cancer patients. Although one might expect QOL to improve with remission, Firkins *et al.* report that mental health issues continue to negatively impact QOL among long-term cancer survivors (7). This link between cancer and mental health is further emphasized by Michoglou *et al.*, who explore the mechanisms connecting depression with pancreatic cancer and highlight the complexities of managing mental health in the context of cancer itself, rather than solely focusing on surgery-related morbidities (8). While pylorus-preserving surgery might be expected to improve QOL by alleviating GI symptoms like dumping syndrome, diarrhea, and weight loss, Ohtsuka *et al.* found that pylorus-preservation has no significant effect on QOL (9). They concluded that psychosocial QOL remains low regardless of the surgical approach, underscoring the need for long-term mental health support, independent of the physiological effects of surgery.

As prognosis and survivorship for pancreatic cancer continue to improve, recognizing that the psychosocial impacts often outweigh the physical consequences of surgical treatment becomes increasingly important. The need for comprehensive support grows to address both the physical and non-physical challenges patients face. In a large survey of cancer survivors, unmet needs related to physical health accounted for less than 40% of all reported needs (10). The remaining unmet needs spanned financial, educational, autonomy-related, healthcare system resources, emotional, mental, interpersonal, societal, existential, and personal identity concerns. Dr. Zhang and colleagues contribute to this evolving understanding of holistic cancer care, demonstrating that post-surgical physical sequelae are generally less disruptive to long-term survivors' QOL than the ongoing socioeconomic and psychological burdens associated with a history of pancreatic cancer. This highlights the need for oncologic surgical care to extend beyond managing post-operative symptoms to include long-term support for the intangible morbidities that persist after curative-intent resection.

In summary, as the field of pancreatic cancer treatment, including its cornerstone treatment modality PD, continues to evolve, we are experiencing a paradigm shift in what defines "best outcomes" for patients. This should include not only objective survival but also the multifaceted factors that contribute to QOL. While scientific, medical, and surgical advancements will continue to enhance post-operative physiologic outcomes and long-term survival, the psychosocial toll of the disease must not be overlooked. A deeper understanding of these non-physical aspects of patient well-being, and the application of this knowledge to develop more nuanced, comprehensive care strategies, should remain a central focus in advancing the field. Pancreatic cancer survivors require more than just surgical intervention—they need and deserve ongoing socioeconomic and psychological support to achieve a meaningful QOL.

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