## Contents

**World Journal of Gastrointestinal Oncology**

*June 15, 2022*  
*Volume 14  Issue 6*

### REVIEW

- **1067** Circular RNAs in hepatocellular carcinoma: Recent advances  
  *Niu ZS, Wang WH*

- **1086** Practical considerations for colorectal cancer screening in older adults  
  *Gornick D, Kadakuntla A, Trovato A, Stetzer R, Tadros M*

- **1103** Fibrolamellar hepatocellular carcinoma: A rare but unpleasant event  
  *Abdelhamed W, El-Kassas M*

### MINIREVIEWS

- **1115** Can dietary flavonoids be useful in the personalized treatment of colorectal cancer?  
  *Pereira-Wilson C*

### ORIGINAL ARTICLE

#### Basic Study

- **1124** Glutamine deprivation impairs function of infiltrating CD8^+^ T cells in hepatocellular carcinoma by inducing mitochondrial damage and apoptosis  
  *Wang W, Guo MN, Li N, Pang DQ, Wu JH*

#### Retrospective Cohort Study

- **1141** Does the addition of Braun anastomosis to Billroth II reconstruction on laparoscopic-assisted distal gastrectomy benefit patients?  
  *Li XG, Song QY, Wu D, Li S, Zhang BL, Zhang LY, Guan D, Wang XX, Liu L*

- **1148** Contemporary, national patterns of surgery after preoperative therapy for stage II/III rectal adenocarcinoma  
  *Soriano C, Bahnson HT, Kaplan JA, Lin B, Moonka R, Pham HT, Kennecke HF, Simianu V*

#### Retrospective Study

- **1162** Clinicopathological differences, risk factors and prognostic scores for western patients with intestinal and diffuse-type gastric cancer  
  *Díaz del Arco C, Estrada Muñoz L, Ortega Medina L, Molina Roldán E, Cerón Nieto MÁ, García Gómez de las Heras S, Fernández Aceñero MJ*

#### Observational Study

- **1175** Characterizing the patient experience during neoadjuvant therapy for pancreatic ductal adenocarcinoma: A qualitative study  
Contents

Randomized Controlled Trial
1187  Biofeedback therapy combined with Baduanjin on quality of life and gastrointestinal hormone level in patients with colorectal cancer
  Zhou XD, Wei HG, Ai FL

META-ANALYSIS
1199  Does chronic kidney disease affect the complications and prognosis of patients after primary colorectal cancer surgery?
  Liu XY, Zhang B, Cheng YX, Tao W, Yuan C, Wei ZQ, Peng D

LETTER TO THE EDITOR
1210  Hepatocellular carcinoma and immunotherapy: Beyond immune checkpoint inhibitors
  Abushukair HM, Saeed A
1213  Insight on BRAF<sup>V600E</sup> mutated colorectal cancer immune microenvironment
  Abushukair HM, Zaitoun SM, Saeed A

CORRECTION
1216  Correction to "MicroRNA-320a suppresses tumor progression by targeting PBX3 in gastric cancer and is downregulated by DNA methylation"
  Li YS, Zou Y, Dai DQ
ABOUT COVER
Editorial Board Member of World Journal of Gastrointestinal Oncology, Tamás Micsik, MD, PhD, Assistant Professor, The First Department of Pathology and Experimental Cancer Research, Semmelweis University Budapest, Budapest h-1085, Hungary. micsikt@gmail.com

AIMS AND SCOPE
The primary aim of World Journal of Gastrointestinal Oncology (WJGO, World J Gastrointest Oncol) is to provide scholars and readers from various fields of gastrointestinal oncology with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

WJGO mainly publishes articles reporting research results and findings obtained in the field of gastrointestinal oncology and covering a wide range of topics including liver cell adenoma, gastric neoplasms, appendiceal neoplasms, biliary tract neoplasms, hepatocellular carcinoma, pancreatic carcinoma, cecal neoplasms, colonic neoplasms, colorectal neoplasms, duodenal neoplasms, esophageal neoplasms, gallbladder neoplasms, etc.

INDEXING/ABSTRACTING
The WJGO is now indexed in Science Citation Index Expanded (also known as SciSearch®), PubMed, PubMed Central, and Scopus. The 2021 edition of Journal Citation Reports® cites the 2020 impact factor (IF) for WJGO as 3.393; IF without journal self cites: 3.333; 5-year IF: 3.519; Journal Citation Indicator: 0.5; Ranking: 163 among 242 journals in oncology; Quartile category: Q3; Ranking: 60 among 92 journals in gastroenterology and hepatology; and Quartile category: Q3. The WJGO’s CiteScore for 2020 is 3.3 and Scopus CiteScore rank 2020: Gastroenterology is 70/136.

RESPONSIBLE EDITORS FOR THIS ISSUE
Production Editor: Ying-Yi Yuan; Production Department Director: Xiang Li; Editorial Office Director: Ya-Juan Ma.

NAME OF JOURNAL
World Journal of Gastrointestinal Oncology

ISSN
ISSN 1948-5204 (online)

LAUNCH DATE
February 15, 2009

FREQUENCY
Monthly

EDITORS-IN-CHIEF
Monjur Ahmed, Florin Burada

EDITORIAL BOARD MEMBERS

PUBLICATION DATE
June 15, 2022

COPYRIGHT
© 2022 Baishideng Publishing Group Inc

INSTRUCTIONS TO AUTHORS
https://www.wjgnet.com/bpg/gerinfo/204

GUIDELINES FOR ETHICS DOCUMENTS
https://www.wjgnet.com/bpg/GerInfo/287

GUIDELINES FOR NON-NATIVE SPEAKERS OF ENGLISH
https://www.wjgnet.com/bpg/gerinfo/240

PUBLICATION ETHICS
https://www.wjgnet.com/bpg/GerInfo/288

PUBLICATION MISCONDUCT
https://www.wjgnet.com/bpg/gerinfo/208

ARTICLE PROCESSING CHARGE
https://www.wjgnet.com/bpg/gerinfo/242

STEPS FOR SUBMITTING MANUSCRIPTS
https://www.wjgnet.com/bpg/gerinfo/239

ONLINE SUBMISSION
https://www.f6publishing.com
Observational Study

Characterizing the patient experience during neoadjuvant therapy for pancreatic ductal adenocarcinoma: A qualitative study

Lena Stevens, Zachary J Brown, Ryan Zeh, Christina Monsour, Sharla Wells-Di Gregorio, Heena Santry, Aslam M Ejaz, Timothy Michael Pawlik, Jordan M Cloyd

Specialty type: Oncology

Provenance and peer review: Invited article; Externally peer reviewed.

Peer-review model: Single blind

Peer-review report's scientific quality classification
Grade A (Excellent): 0
Grade B (Very good): B
Grade C (Good): C
Grade D (Fair): 0
Grade E (Poor): 0

P-Reviewer: Falasca M, Australia; Nguyen LT, Viet Nam
A-Editor: Xu ZL

Received: January 14, 2022
Peer-review started: January 14, 2022
First decision: March 13, 2022
Revised: April 1, 2022
Accepted: May 17, 2022
Article in press: May 17, 2022
Published online: June 15, 2022

Abstract

BACKGROUND
Neoadjuvant therapy (NT) has increasingly been utilized for patients with localized pancreatic ductal adenocarcinoma (PDAC). It is the recommended approach for borderline resectable (BR) and locally advanced (LA) cancers and an increasingly utilized option for potentially resectable (PR) disease. Despite its increased use, little research has focused on patient-centered metrics among patients undergoing NT, including patient experiences, preferences, and recommendations. A better understanding of all aspects of the patient experience during NT may identify opportunities to design interventions aimed at improving quality of life; it may also facilitate the completion of NT and receipt of surgery, ultimately optimizing long-term outcomes.

AIM
To understand the experience of patients initiating and receiving NT to identify opportunities to improve neoadjuvant cancer care delivery.

METHODS
Semi-structured interviews of patients with localized PDAC during NT were conducted to explore their experience initiating and receiving NT. Interviews took place between August 2020 and October 2021. Due to the descriptive nature of the research, questions were open ended. Interviews were conducted over the phone, audio recorded and then transcribed. All interviews were coded by two inde-
pendent researchers using NVivo 12, iteratively identifying themes until thematic saturation was achieved. An integrative approach to qualitative analysis was used, utilizing both inductive and deductive methods.

RESULTS
A total of 12 patients with localized PDAC were interviewed. Patients with BR (n = 7), PR (n = 2), and LA (n = 3) cancers participated in the study. All patients indicated that choosing NT was the doctor’s recommendation, while most reported not being familiar with the concept of NT (n = 11) and that NT was presented as the only option (n = 8). Five themes describing the patient experience emerged: physical symptoms, emotional symptoms, coping mechanisms, access to care, and life factors. The most commonly cited recommendation for improving the experience of NT was improved education before and during NT (n = 8). Patients highlighted the need for more information on the rationale behind choosing NT prior to surgery, the anticipated surgery and its likelihood of surgery occurring after NT, as well as general information prior to starting NT treatment. The need for seeing different members of the healthcare team, including ancillary services was also frequently cited as a recommendation for improving the experience of NT (n = 5).

CONCLUSION
This study provides a framework to allow for a better understanding of the PDAC patient experience during NT and highlights opportunities to improve quality and quantity of life outcomes.

Key Words: Pancreatic ductal adenocarcinoma; Neoadjuvant therapy; Patient experience; Patient-centered care; Quality of life; Qualitative research

©The Author(s) 2022. Published by Baishideng Publishing Group Inc. All rights reserved.

Core Tip: This study aims to understand the experience of localized pancreatic ductal adenocarcinoma (PDAC) patients initiating and receiving neoadjuvant therapy (NT). Semi-structured interviews of patients with localized PDAC during NT were conducted; 12 patients were interviewed. All patients indicated that choosing NT was the doctor’s recommendation. Most reported not being familiar with the concept of NT. Five themes describing the patient experience emerged. This study provides a framework to allow for a better understanding of the patient experience and highlights opportunities to improve quality and quantity of life outcomes for patients with PDAC.

URL: https://www.wjgnet.com/1948-5204/full/v14/i6/1175.htm
DOI: https://dx.doi.org/10.4251/wjgo.v14.i6.1175

INTRODUCTION
The delivery of chemotherapy and/or radiation therapy prior to surgery, known as neoadjuvant therapy (NT), is increasingly utilized for patients with pancreatic ductal adenocarcinoma (PDAC)[1,2]. Since a significant proportion of patients are unable to receive all intended adjuvant therapies following major pancreatectomy, NT ensures the receipt of some systemic therapy and leads to improved rates of multimodality therapy. NT also improves margin-negative resection rates, enhances patient selection by ensuring the absence of rapid tumor progression prior to surgery, enables an in vivo test of the efficacy of chemotherapy, and based on emerging evidence from randomized controlled trials, may lead to improved overall survival[3-7]. Based on these advantages, NT is now the recommended approach for borderline resectable (BR) and locally advanced (LA) cancers and an increasingly utilized option for potentially resectable (PR) disease according to national guidelines[3,8,9].

Despite its increasing use in PDAC and other cancer types[2], little is known about the patient experience during NT. Indeed, the neoadjuvant time period might be particularly distressing for patients who must cope with not only the toxicity of treatment, but also side effects from the tumor itself which remains in situ. Furthermore, little is known about the psychosocial impact of NT particularly given many patients’ inherent preference for “just getting the cancer out,” as well as the uncertainty of future surgery[10]. A recent systematic review found scarce data on quality of life (QOL) during NT for
PDAC and no existing literature on other aspects of the patient experience[11]. In contrast to immediate surgery, NT is also inherently multi-disciplinary in nature. As such, there may be barriers to effective care initiation and coordination that impede the completion of all scheduled therapy and the receipt of surgical resection[12].

Therefore, the purpose of this qualitative study was to characterize the patient experience during NT for PDAC. Specifically, we sought to understand patient treatment preferences, information needs, the physical and psychosocial impact of treatment, and barriers to successful initiation and delivery of NT. A better understanding of all aspects of the patient experience during NT may identify opportunities to design interventions aimed at improving QOL during NT, facilitating completion of NT and receipt of surgery, and ultimately optimizing the long-term outcomes of patients with PDAC.

MATERIALS AND METHODS

Study design and population
Patients with PDAC undergoing NT prior to planned surgery in the future were recruited to participate in this qualitative study. All treatment decisions at our institution are made at a pancreatic cancer specialty specific multidisciplinary clinic and made on an individualized basis. Participants were identified by prospectively screening ambulatory clinics at The Ohio State University Wexner Medical Center and James Comprehensive Cancer Center. Inclusion criteria included receiving at least two cycles of chemotherapy in a neoadjuvant intent, still eligible for surgical resection, and English language speaking, without restrictions on age, race, or disability. Eligible patients were contacted by phone, informed consent was obtained, and an interview was scheduled at the participant’s convenience. Due to the COVID-19 pandemic, interviews were conducted by phone between August 2020 and October 2021.

Interview guide and process
The interview script was developed using evidence synthesis, stakeholder engagement, and expert opinion. The content of the interviews focused on patient treatment preferences, perspectives on the decision-making process, and all aspects of the patient experience during NT; recommendations on opportunities to improve the delivery of NT were also sought. Questions were open-ended, prompting additional questions depending on the responses of the interviewees (Supplementary material). This type of interview method was selected due to the descriptive nature of the research. Semi-structured interviews allow researchers to discuss topics of interest more in detail by elaborating on emerging themes and asking probing questions. A nominal gift card was given to participants for their participation. This study was approved by the Institutional Review Board of The Ohio State University (IRB# 2019C0155).

Statistical analysis
All interviews occurred by phone, were audio recorded, and then manually transcribed verbatim by the researchers. Transcripts were then uploaded to NVivo12 (QSR International, Australia) for data extraction, synthesis, and analysis purposes. Data extraction followed an integrated approach, including both an inductive and deductive coding methodology[13]. The following preliminary codes were developed before a more in-depth, inductive coding process took place: Patient Experiences; Patient Perspectives on NT; Solutions, Facilitators and Recommendations; and Sources of Information. Two researchers independently coded the transcripts for sub-themes in an iterative fashion until thematic saturation was achieved[13]. Interviews were then re-reviewed and coded using the final codebook. When coding from both independent researchers was not concordant, these instances were reviewed with a third researcher at team meetings. These sections and codes were discussed until a consensus was reached. Demographic data from participants were summarized and illustrative quotes in each theme were selected.

RESULTS

Participant characteristics
A total of 12 patients participated in the interviews. On average, patients were 67 years old, ranging from 52 to 81 years. Patients with BR (n = 7, 58%), PR (n = 2, 17%), and LA (n = 3, 25%) cancers participated in the study. A majority of patients (n = 7, 58%) received chemotherapy and radiation therapy before their planned surgery while others (n = 5, 42%) received just chemotherapy. At most recent follow-up, most patients (n = 10, 83%) had completed NT with 8 patients (67%) undergoing surgical resection of their tumor. Complete participant characteristics are reported in Table 1.
Table 1 Participant characteristics (n = 12)

<table>
<thead>
<tr>
<th>Variable</th>
<th>Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Age [mean (range), yr]</td>
<td>67 (52 – 81)</td>
</tr>
<tr>
<td>Gender</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>8 (67)</td>
</tr>
<tr>
<td>Female</td>
<td>4 (33)</td>
</tr>
<tr>
<td>Race</td>
<td></td>
</tr>
<tr>
<td>White</td>
<td>9 (75)</td>
</tr>
<tr>
<td>Black</td>
<td>3 (25)</td>
</tr>
<tr>
<td>Marital status</td>
<td></td>
</tr>
<tr>
<td>Married</td>
<td>7 (58)</td>
</tr>
<tr>
<td>Single</td>
<td>4 (33)</td>
</tr>
<tr>
<td>Divorced</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Stage of cancer</td>
<td></td>
</tr>
<tr>
<td>PR</td>
<td>2 (17)</td>
</tr>
<tr>
<td>BR</td>
<td>7 (58)</td>
</tr>
<tr>
<td>LA</td>
<td>3 (25)</td>
</tr>
<tr>
<td>Location of tumor</td>
<td></td>
</tr>
<tr>
<td>Head</td>
<td>9 (75)</td>
</tr>
<tr>
<td>Body</td>
<td>2 (17)</td>
</tr>
<tr>
<td>Neck</td>
<td>1 (8)</td>
</tr>
<tr>
<td>Type of NT</td>
<td></td>
</tr>
<tr>
<td>Chemo</td>
<td>5 (42)</td>
</tr>
<tr>
<td>Chemo + XRT</td>
<td>7 (58)</td>
</tr>
<tr>
<td>Length of NT</td>
<td></td>
</tr>
<tr>
<td>&lt; 3 mo</td>
<td>1 (10)</td>
</tr>
<tr>
<td>3-6 mo</td>
<td>6 (60)</td>
</tr>
<tr>
<td>&gt; 6 mo</td>
<td>3 (30)</td>
</tr>
<tr>
<td>Type of chemo</td>
<td></td>
</tr>
<tr>
<td>FOLFIRINOX</td>
<td>4 (33)</td>
</tr>
<tr>
<td>Gemcitabine/nab-paclitaxel</td>
<td>2 (17)</td>
</tr>
<tr>
<td>Other/both</td>
<td>6 (50)</td>
</tr>
<tr>
<td>Major complications during NT</td>
<td></td>
</tr>
<tr>
<td>Hospitalization</td>
<td>2 (50)</td>
</tr>
<tr>
<td>ER visit, no admission</td>
<td>1 (25)</td>
</tr>
<tr>
<td>Other</td>
<td>1 (25)</td>
</tr>
<tr>
<td>Travel distance</td>
<td></td>
</tr>
<tr>
<td>&lt; 15 miles</td>
<td>4 (33)</td>
</tr>
<tr>
<td>15 – 30 miles</td>
<td>1 (8)</td>
</tr>
<tr>
<td>31 – 50 miles</td>
<td>2 (17)</td>
</tr>
<tr>
<td>51 – 100 miles</td>
<td>3 (25)</td>
</tr>
<tr>
<td>100+ miles</td>
<td>2 (17)</td>
</tr>
</tbody>
</table>
Stevens L et al. Patient experience during NT for PDAC

Patient perspectives on neoadjuvant therapy

Among the 12 patients who participated in the interviews, the vast majority (n = 11, 92%) were not familiar with the concept of NT at the time of initial consultation. All subjects reported that NT was the doctor’s recommendation and most (n = 8, 67%) explained that NT was presented to them as the only option. All interviewees indicated that improving resectability was the main rationale for choosing NT. While some (n = 6, 50%) patients indicated that before meeting with their physicians they did not have a preference for a specific treatment plan, others (n = 4, 33%) expressed that they had hoped to avoid chemotherapy and undergo upfront surgery. All patients indicated that their main source of information were members of their health care team while other sources of information discussed included the internet (n = 4, 33%), family and friends (n = 3, 25%), and educational materials (n = 1, 8%).

Patient experience during neoadjuvant therapy

Five subthemes of patient experiences during NT emerged: physical symptoms, emotional symptoms, coping mechanisms, access to care, and life factors (Figure 1 and Table 2). All participants reported elements of each of the five subthemes.

Physical symptoms: A few patients (n = 3, 25%) discussed that they did not experience any major side effects and they were tolerating their therapy well (“I have never had any symptoms. No throwing up, no nothing.”). However, most patients reported experiencing major side effects from their treatment. Many patients reported feeling weak (n = 6, 50%). One patient stated: “I’ll say at night, I am going to do this, that and the other and the next day comes and my body says ‘no, we’re not going to do that’.” Others mentioned challenges around weight loss, loss of appetite, and the taste of food (n = 5, 42%), as well as a general feeling of sickness (n = 4, 33%) (“After getting chemo for the next 5 days I’m sick as a dog.”).

Emotional symptoms: In addition to shock experienced during their diagnosis, patients reported varying rates of fear and depression (“… it scared me. It depressed me.”). A few patients (n = 3, 25%) shared concerns for their family and friends’ well-being, regarding uncertainty about next steps in treatment, and about their overall prognosis. One patient stated: “I love my wife and I want to be around for her. It’s hard.” Some (n = 3, 25%) also shared not wanting to think about and dwell too much on their diagnosis and treatment approach, as well as the need for not too much information, as it leads to unnecessary anxiety.

Coping and support mechanism: The main coping and support mechanism cited by most patients (n = 10, 83%) was support from family members. Tangible aspects of support included family members and friends offering rides to appointments, discussing different treatment options, helping with coordinating care and reaching out to the medical team, as well as helping with chores around the house. Patients putting their trust in their religious faith was another coping and support mechanism mentioned by some (n = 5, 42%). One patient stated: “I’m a religious person, so that’s enough said.” Several patients (n = 4, 33%) also mentioned receiving support from different members of the medical team (“So, there is always someone here to answer my questions, which also feels good and gives you comfort.”).
Table 2 Representative quotes describing patient experience during neoadjuvant therapy

| Physical symptoms | Quote No. 1 | “After getting chemo for the next 5 d I’m sick as a dog, weak, losing weight, lost about 40 lbs.” |
| Physical symptoms | Quote No. 2 | “Side effects of course. You’re gonna be queasy, you’re gonna be lightheaded. Definitely, I ate, but food didn’t taste good, even water didn’t taste good and I didn’t expect that.” |
| Physical symptoms | Quote No. 3 | “I’m tired all the time. No energy. I sleep a lot. A little diarrhea. Pretty mild, never threw up yet. Only real bad thing is my appetite. Lost it about completely I have to force myself to eat until I start gagging” |
| Emotional symptoms | Quote No. 1 | “Most times I don’t care, I really just don’t want to think about it. I just want to watch a good movie. You know what I mean. Not dwell on it all the time. I love my wife and I want to be around for her. It’s hard.” |
| Emotional symptoms | Quote No. 2 | “There are days that I get a little depressed. Because… I am used to movement. And I just don’t have the stamina, nor the willpower.” |
| Coping and support mechanisms | Quote No. 1 | “…my wife and I, we are Christians and we know it’s up to him, the Lord.” |
| Coping and support mechanisms | Quote No. 2 | “I have good support from my family and friends. And prayer circles. Getting financial gifts to help us with gas money and things like that. So, they’ve all been very supportive.” |
| Access to care | Quote No. 1 | “And I have had a lot of friends that make sure that I get to my treatments. So, I don’t have any problems there.” |
| Access to care | Quote No. 2 | “But it got to be a little bit much for [my sister-in-law] so, I had to withdraw money to get me through this [to ride the bus] that was an extra expense, as I am a senior. And I’m on a fixed income. So, I hadn’t counted on that.” |
| Access to care | Quote No. 3 | “I have no problem with transportation. My wife was always there to give me a ride.” |
| Life factors | Quote No. 1 | “I have help with paying my bills, [grocery store], cleaning my house, things like that, doing laundry. So, I am very lucky.” |
| Life factors | Quote No. 2 | “I worry about all the damn bills” |
| Life factors | Quote No. 3 | “I’m retired so really the work thing didn’t come into play, but I have chores around the house that I’m limited in doing” |

**Access to care:** For most, access and coordination was an important but feasible aspect of NT. This included minimal obstacles associated with traveling to medical appointments (n = 8, 67%), scheduling appointments (n = 6, 50%), contacting doctors (n = 6, 50%), getting answers to questions (n = 4, 33%), getting insurance to cover treatments (n = 3, 25%), or seeing a doctor and getting referrals (n = 2, 17%). While in general patients did not experience major complications accessing and coordinating care, a minority of patients reported some barriers. A few (n = 3, 25%) highlighted that traveling to appointments was burdensome. One patient explained: “Every time we have to have something done, it’s two hours out of our day, about 2.5 h out of our day just driving to the place. But we made that choice knowing that was the case for the care, the treatment and we’ve been proceeding.”

**Life factors:** Finally, all patients described the need to integrate their treatment and condition with their normal life circumstances. Several patients discussed the impact of NT on other aspects of their life. NT impacting a patient’s work and financial situation were the most commonly cited sub-themes. Many patients discussed that missing work was not a major challenge they were faced with (n = 5, 42%), and that they did not experience major financial concerns (n = 6, 50%). Yet, some (n = 3, 25%) expressed concern around not being able to work and the burden it placed on them financially (n = 4, 33%). One patient stated: “I’ve been off since all this happened (…) drives me kinda nuts. I used to work all the time. But I got no energy now.” Another patient explained: “I had to withdraw money to get me through this that was an extra expense, as I am a senior. And I’m on a fixed income. So, I hadn’t counted on that.” Other life aspects mentioned were patients having to deal with other health problems (n = 1, 8%) at the same time they are on NT and needing help with daily activities (n = 2, 17%).

**Recommendations for improving the experience of neoadjuvant therapy**
The most commonly cited recommendation for improving the experience of NT was to provide better
education and more information on NT (n = 7, 58%). Patients highlighted the need for more information on: the rationale behind choosing NT prior to surgery, the anticipated surgery and its likelihood of occurring after NT, as well as general information prior to starting NT treatment. Patients also discussed that more discussions with physicians could potentially be helpful, but also highlighted the need for information tailoring (not too much vs not too little). The need for seeing different members of the healthcare team, including ancillary services was also frequently cited as a recommendation for improving the experience of NT (n = 5, 42%). Patients discussed the importance of seeing psychologists, palliative care doctors, case workers, physical therapists, and nutritionists. Better coordination and communication (n = 2, 17%) and better treatments (n = 2, 17%) were also offered as potential recommendations.

DISCUSSION
Pancreatic ductal adenocarcinoma is a highly aggressive malignancy, often thought of as a systemic disease at the time of diagnosis, that requires multimodal therapy with a combination of surgery and chemotherapy in order to achieve meaningful long-term survival[14-17]. NT is being increasingly utilized in patients with localized PDAC[1,3,18]. Previous research on NT for PDAC has focused on its safety, efficacy, and cost-effectiveness with little data on patient-centered preferences or experiences during NT. In this qualitative study of patients actively receiving NT for PDAC, we found several important observations. First, patients are generally unfamiliar with the concept of NT prior to meeting with an oncologist. While many have an inherent preference for upfront surgery, most understand their providers’ recommendation for NT as an attempt to improve resectability (or likelihood of achieving margin-negative resection). Second, patients have unique experiences and care needs during NT that providers should be aware of in order to optimize patient-centered outcomes. A patient-centered approach that supports physical and emotional symptoms and recognizes the importance of life integration is required. Third, specific recommendations for improving the experience of NT prior to surgery were identified.

Interestingly, although patients in our study were actively receiving NT, most were relatively unfamiliar with the concept of NT. All patients expressed that NT was the recommendation of their doctor. While a few patients expressed their desire for a surgery-first approach or to avoid chemotherapy altogether, nevertheless, all patients eventually came to understand and agree with the rationale for NT. This may highlight a disconnect between patients and providers in that systemic chemotherapy is part of the treatment of all patients with pancreatic cancer as even patients with localized cancers who have undergone resection are likely to experience disease recurrence[19,20]. Similar results were found in patients with breast cancer. A study in women with breast cancer who underwent NT found a majority of women understood that chemotherapy was given prior to surgery in order to shrink the tumor but did not grasp the concept that chemotherapy is utilized to treat systemic disease beyond simply local tumor control[21].
Missing from prior studies has been an evaluation of patient-centered preferences and outcomes regarding the use of NT for PDAC. Cancer-related treatment decisions are complex and require consideration of multiple factors; such decisions are often made in the context of shared decision making (SDM), a model in which informed and engaged patients make health-care decisions in conjunction with their providers[22]. The degree to which patients are involved in the SDM process of choosing NT or immediate surgery is unclear. Most patients with cancer desire an active role in making decisions about their care[22] and such patient-centered decision making has been shown to improve patients’ understanding of their treatment options, satisfaction with their health care, and overall quality of life (QOL)[24-26]. Previous research in breast and rectal cancer suggest patient-centered approaches to SDM regarding NT are lacking in clinical practice[27-29]. Indeed, SDM is under-utilized by surgeons in general[30]. Additionally, it is well known that strong emotions and fears may influence treatment decision making[31]. Specifically, emotions may cause behavior or decisions to diverge from more rational or practical decision making consistent with one’s values[32]. For example, patients state their desire to “just get the cancer out” even if this emotional response does not align with one’s values, priorities, or optimal treatment strategy. We found most patients believed NT was their only treatment option moving forward. This is not surprising as a majority of the patients in our study had either BR or LA disease which is currently the preferred treatment strategy based on recent randomized controlled trials[33,34]. Another study has found that most patients believed there was no other treatment option and thus accepted NT[21]. Understanding patient preferences, values, and expectations regarding NT will improve SDM which will lead to not only delivering patient-centered care but also the opportunity to overcome barriers to patient acceptance of NT.

While not previously studied in PDAC, in practice, multiple barriers to the use of NT are often expressed by patients. For example, some patients may have financial concerns secondary to missing work by “delaying” surgery. Others worry about arranging and/or affording transportation for NT due to long travel distances. Additionally, in our study, most, if not all patients, experienced physical and emotional symptoms during NT. Furthermore, the development of toxicities during the course of NT may prove to be a potential barrier that may worsen a patient’s ability to subsequently undergo an operation. A meta-analysis of 38 studies of which 1738 patients received NT found approximately 64% of patients experienced at least grade III toxicity[35]. In fact, this number may be magnified at community hospitals which may not have the same resources as tertiary referral centers to manage toxicities and progress patients through therapy[36-38].

We found that patients with PDAC receiving NT must balance their cancer treatment with other aspects of their lives such as family responsibilities and work in addition to coping with the physical and emotional symptoms that accompany their new diagnosis and treatment (Figure 1). These findings are similar to a previous qualitative study of patients with breast cancer receiving NT. Beaver et al[21] reported five themes among women receiving NT: Coping with the rapid transition from “well” to “ill”, information needs and decision making, needing support and empathy, impact on family, and creating a new “normal”. These findings suggest similar experiences among patients receiving chemotherapy prior to surgery regardless of cancer type. While patients with PDAC certainly have unique challenges such as biliary obstruction, malnutrition, gastric outlet obstruction, as well as cancer-related pain, additional research is needed on supporting the general care needs directly influenced by the neoadjuvant aspects of treatment.

The findings from our study provide a framework to allow for a better understanding of the patient experience during NT and highlight opportunities for inter-disciplinary interventions to improve patient-centered outcomes of those with PDAC. Indeed, many patients who receive NT fail to either complete NT or to undergo subsequent pancreatectomy with common reasons including disease progression or worsening performance status due to toxicity[33,39,40]. Furthermore, since failing to complete therapy or undergo surgical resection is associated with a worse prognosis, having a patient-centered approach to understand potential barriers to completion is essential. As we have demonstrated in this study, patients experience both physical and emotional symptoms during treatment and require a team approach with the help of ancillary services to help complete therapy. Involvement of patient navigators, social workers, nutritionists, and physical therapists to address patient concerns and symptoms may aid to improve the high attrition rate in patients receiving NT. Previous research has highlighted patient dissatisfaction with the lack of access to counseling services, support groups, and educational tools[41].

There are several limitations to our study. Although our study reached theme saturation, the relatively small sample size and single institution design means that the findings may not be generalizable to all patients with PDAC who are receiving NT. Additionally, our study includes patients with PR, BR and LA disease where larger sample sizes are required to investigate if the patient experience differs according to anatomic stage (e.g., patients with LA disease may have lower expectations of undergoing resection and/or greater burden of cancer-related symptoms than patients with PR disease.) Finally, it is unclear if the patient experience is temporal-dependent and since interviews were performed at a single time during NT, future research may focus on longitudinal evaluations of the patient experience.
CONCLUSION

In conclusion, this is the first qualitative study to characterize the experience of patient’s receiving NT for localized PDAC. Our findings clarify the lack of familiarity with the concept of NT prior to initiating treatment, the unique care needs of patients receiving NT, and recommendations to improve the delivery of cancer care in the neoadjuvant setting. These data provide a framework to allow for a better understanding of the patient experience during NT and highlight opportunities for patient-centered interventions aimed at improving quality and quantity of life outcomes of those with PDAC.

ARTICLE HIGHLIGHTS

Research background
Neoadjuvant therapy (NT) has increasingly been utilized for patients with localized pancreatic ductal adenocarcinoma (PDAC). It is the recommended approach for borderline resectable (BR) and locally advanced (LA) and it has also increasingly been utilized for potentially resectable (PR) disease. However, little research has focused on patient-centered metrics among patients undergoing NT, including patient experiences, preferences, and recommendations.

Research motivation
A better understanding of all aspects of the patient experience during NT may help identify opportunities to design interventions aimed at improving quality of life. It may also facilitate the completion of NT and receipt of surgery, ultimately optimizing long-term outcomes.

Research objectives
This research aims to understand the experience of patients initiating and receiving NT to identify opportunities to improve neoadjuvant cancer care delivery.

Research methods
Semi-structured, open-ended interviews of patients with localized PDAC during NT were conducted to explore their experience initiating and receiving NT. Interviews were conducted over the phone. All interviews were audio recorded, transcribed, and coded by two independent researchers using NVivo 12, iteratively identifying themes until thematic saturation was achieved.

Research results
A total of 12 patients with localized PDAC were interviewed. All patients indicated that choosing NT was the doctor’s recommendation and most reported not being familiar with the concept of NT (n = 11, 92%). Five patient experience themes emerged: physical symptoms, emotional symptoms, coping mechanisms, access to care, and life factors. Improved education before and during NT was the most commonly cited recommendation for improving the experience during NT (n = 7, 58%). Patients highlighted the need for more information on the rationale behind choosing NT prior to surgery, the anticipated surgery and its likelihood of surgery occurring after NT, as well as general information prior to starting NT treatment.

Research conclusions
This study provides a framework to allow for a better understanding of the PDAC patient experience during NT and highlights opportunities to improve quality and quantity of life outcomes.

Research perspectives
This exploratory research utilizes qualitative interviews to examine the patient experience when initiating and receiving NT.

ACKNOWLEDGEMENTS

The authors extend their sincere appreciation to all participants of this study who shared their experience with us. We thank Angela Sarna for her assistance with participant recruitment and administrative support. The content is solely the responsibility of the authors and does not necessarily represent the official views of the National Center for Advancing Translational Sciences or the National Institutes of Health.
FOOTNOTES

Author contributions: Cloyd JM designed the research study; Stevens L, Zeh R, Monsour C and Cloyd JM performed the research; Stevens L, Brown ZJ and Cloyd JM analyzed the data and wrote the manuscript; Wells-Di Gregorio S, Santry H, Ejaz AM and Pawlik TM provided expert opinion and edits to the manuscript; and All authors have read and approve the final manuscript.

Institutional review board statement: The study was reviewed and approved by the Institutional Review Board of The Ohio State University.

Informed consent statement: All study participants provided informed verbal consent prior to study enrollment.

Conflict-of-interest statement: There are no conflicts of interest to report.

Data sharing statement: No additional data are available.

STROBE statement: The authors have read the STROBE Statement – checklist of items, and the manuscript was prepared and revised according to the STROBE Statement – checklist of items.

Open-Access: This article is an open-access article that was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution NonCommercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: https://creativecommons.org/Licenses/by-nc/4.0/.

Country/Territory of origin: United States

ORCID number: Lena Stevens 0000-0002-0958-0035; Zachary J Brown 0000-0003-1899-5467; Ryan Zeh 0000-0003-2746-289X; Christina Monsour 0000-0002-7003-3751; Sharla Wells-Di Gregorio 0000-0002-5193-7448; Heena Santry 0000-0003-2352-1557; Aslam M Ejaz 0000-0002-1387-2604; Timothy Michael Pawlik 0000-0002-4828-8096; Jordan M Cloyd 0000-0002-2373-8433.

S-Editor: Ma YJ
L-Editor: A
P-Editor: Ma YJ

REFERENCES


Bradley EH, Curry LA, Devers KJ. Qualitative data analysis for health services research: developing taxonomy, themes, and theory. Health Serv Res 2007; 42: 1758-1772 [PMID: 17286625 DOI: 10.1111/j.1475-6770.2006.00684.x]


