

Patients' Descriptions of Initial Symptoms of Cholangiocarcinoma and the Journey to Diagnosis: A Qualitative Study

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Abstract

Introduction: Cholangiocarcinoma (CCA) is a rare cancer that is clinically silent in many patients and otherwise largely presents with non-specific symptoms. Most patients are therefore diagnosed at advanced stages.

Objective: The aim of this study was to gain knowledge of patients' descriptions of initial symptoms of disease, their help-seeking behaviour and experience of the subsequent journey to diagnosis.

Methods: This was explored in a qualitative descriptive study with semi-structured interviews (n=15). We analyzed data using content analysis with an inductive approach.

Results: Three themes emerged: 1: Experiencing non-specific, vague or specific symptoms: Participants experiencing non-specific symptoms tended to delay seeing their general practitioner (GP), while specific symptoms, particularly jaundice, prompted urgent GP contact. 2: Experiencing a swift versus prolonged diagnosis: participants with specific symptoms were overall swiftly referred to diagnostic testing at specialized centers while some participants with non-specific symptoms experienced a prolonged and complicated journey to diagnosis. 3: "Being in the know" during the diagnostic journey: Concrete and consistent information facilitated trust and a sense of control.

Conclusion: Campaigns sanctioning prompt help-seeking behavior for non-specific, concerning symptoms may accelerate help-seeking and potentially, detection of rare cancers such as CCA. GP elicitation of symptoms that are normalized or downplayed by patients may also facilitate earlier detection. Patient navigators could ensure the

informational needs of CCA patients on the journey to diagnosis.

Keywords: Cholangiocarcinoma; Diagnosis; Patient's descriptions; Initial symptoms; Qualitative

Introduction

Cholangiocarcinoma (CCA) is a rare cancer originating from the bile ducts [1,2]. It is the second most common primary hepatic tumour and accounts for nearly 3% of all gastrointestinal cancers diagnosed worldwide [3]. Two-thirds of CCAs remain clinically silent and remaining cases often present with nonspecific symptoms such as weight loss, abdominal pain, night sweats, and fatigue [4]. This makes the diagnosis of CCA challenging and the majority of patients are diagnosed at late stages [5-8]. There are indications that the incidence of CCA, specifically intrahepatic CCA, is increasing in the UK and USA [3,9]. CCA commonly occurs in the middle-aged and elderly and is more prevalent in men [3]. The highest incidence rate is found in men and women resident in the most deprived socio-economic quintile in UK [9]. Surgical resection remains the mainstay curative treatment, however less than one-third of patients are radically resected [7]. Despite advances in surgical and palliative treatment, CCA therefore remains associated with a dismal prognosis [7,8].

Early help-seeking behaviour and timely referral for diagnostic testing is critical for improving survival in patients with cancer [10,11]. In recent years, national recommendations for cancer treatment have focused on acceleration of the diagnostic pathway for patients referred by GPs at suspicion of cancer [12]. There has been less focus on the "pre-referral" period from initial symptoms registered by the patient to the patient's first presentation of symptoms to their GP [13]. Studies across various cancer populations indicate that a complex array of patient-related factors, for

example poor knowledge, lacking awareness, non-recognition of early symptoms among others, contribute to delayed GP consultation at this stage [14,15].

The silent and non-specific nature of presenting symptoms in patients with CCA coupled with the fact that CCA is an extremely rare cancer challenges diagnosis. No studies have qualitatively explored patients' descriptions of initial symptoms of CCA, initial help-seeking behaviour and the journey to diagnosis. Such insight might identify focus areas for quality improvement initiatives at this stage of the disease trajectory. The aim of the study was consequently to explore CCA patients' descriptions of early symptoms of disease, initial help-seeking behaviour, and the journey to diagnosis.

Methods

Design

A qualitative descriptive study was conducted within the perspective of Gadamerian hermeneutics [16]. We collected data through interviews using a semi-structured interview guide designed to tease out CCA patients' descriptions of initial symptoms of disease, initial help-seeking and the journey to diagnosis.

Participants

Participants were recruited from a specialized referral center in the Capital Region of Denmark. We used purposive sampling [17] to achieve a varied sample in regard to age and gender [18]. Inclusion criteria were adults 18 years old and above, having received a diagnosis of CCA within the last 10 months, sufficient language proficiency, having received curative or palliative treatment at the specialized referral center in The Capital Region of Denmark. We excluded patients with last terminal stage cancer. A total of 23 patients were invited to participate in the study, all of which accepted. Rapid disease progression however subsequently prevented 8 from participating in the interviews, leaving a total of 15 participants. Nine participants were interviewed in connection with chemotherapy treatment; 1 in connection with a routine follow-up consultation; 1 at home; and finally 4 came to the hospital specifically for the interviews. All participants were receiving treatment with chemotherapy at the time of their interviews. The median age of participants was 67 years (range 36-82), 7 were females, 5 were employed and 2 were single. The median time since diagnosis of CCA was 4 months, (range 3-8). Five participants received palliative chemotherapy, 7 had undergone explorative laparotomy and palliative chemotherapy, and, finally, 3 participants radical surgery and adjuvant chemotherapy.

Data collection

Prior to interviewing participants we developed an interview guide. The interview guide addressed patients' descriptions of early symptoms and reactions to them, health-seeking behaviour and the diagnostic journey [7,18]. The interview

guide followed the questioning route described by Crabtree & Miller [19]. The first and third author conducted interviews which took place from June 2013 to January 2014. The interviews lasted from 25-50 min. We recruited participants until we deemed data were saturated [20].

Analysis

All interviews were digitally recorded and transcribed verbatim by a trained research assistant. The first, second and third authors individually analysed the interview data using qualitative content analysis with an inductive approach as described by Elo and Kyngäs [21] and Graneheim and Lundman [22]. This entailed the following steps: 1. Reading the interviews to get a sense of whole, 2. Coding units of meaning and creating sub-categories, 3. Collapsing sub-categories into main categories [21]. To substantiate that emerging categories were empirically grounded, the authors continuously moved back and forth between the original interview data and sub-categories and categories [22]. Final consensus for the analysis was reached through discussion, and to increase credibility and dependability, the analysis was discussed with the last author who did not participate in the interviews.

Ethics Approval

Participants consented to participate after receiving written and oral information about the study. They were ensured that participation was voluntary and that they could withdraw from the study at any time. Participants were provided with the option to contact the first author if any questions concerning their condition, treatment or otherwise arose after interviews. The study was approved by the Danish Data Protection Agency (2007-58-0015), The Central Science Ethics Committee in the Capital Region of Denmark (H-4-2013-FSP) and performed in compliance with the Helsinki Declaration [23].

Results

Analysis of the interviews resulted in three themes; Experiencing non-specific, vague symptoms or specific symptoms; Experiencing a swift versus prolonged journey to diagnosis; "Being in the know" during the journey to diagnosis.

Experiencing non-specific, vague or specific symptoms

Many participants recalled the first experienced symptoms as vague and non-specific while others described specific debut symptoms. Non-specific symptoms included feeling more tired than usual, feeling down, itching, non-specific fluctuating pains, periodic fever, decreased appetite, and, notably, for many absence of pain. Vague, non-specific symptoms, stand-alone or in combination, combined with an absence of pain were appraised as mildly concerning. Participants adopted a "let's wait and see" approach rather than consulting their GP. Because the symptoms were so vague they found them difficult to describe to a GP and they worried

that the symptoms were not serious or specific enough to book a GP consultation.

"The week before I didn't feel well. I wasn't on top, but how can you tell your GP that? I don't feel so good - I'm a little tired. It's difficult to say to your GP right? I don't feel well - I'm a little tired. I mean those aren't symptoms you can really use." (P8).

Some participants downplayed non-specific symptoms or attributed them to being busy, stressed, and not eating regularly. Some justified not seeing their GP with the fact that they did not experience any pain.

"I didn't experience any pain - nothing." (P9).

For some, concerned spouses played an important role in encouraging and even forcing participants to see their GP rather than waiting and seeing, attributing the symptoms to being busy or stressed, or hoping that the symptoms would simply go away.

"...And my wife kept on asking me to see my GP and he took a blood sample and that's how he (the GP) found out." (P2).

Jaundice was the debut symptom, often initially noticed by family or friends rather than the participant. All participants viewed jaundice to be a critical symptom of something being wrong and led them to seek urgent medical help. Jaundice occurring in combination with already existing vague symptoms likewise prompted participants to immediately contact their GP. Substantial and unexplained weight loss was a specific symptom leading to GP contact for some participants, in some cases spurred by a spouse or family member, while others initially attributed the weight loss to being stressed, not eating healthy food etc. Weight loss combined with jaundice prompted immediate GP contact.

"And when I started to lose weight- quite a lot -I nearly lost 20 kilos in a year. That was when I decided to see my GP" (P3).

Experiencing a swift versus prolonged journey to diagnosis

When seeking medical help, participants described that they encountered varying reactions from their GPs. Some described their GP as having a "thinking out of the box" approach to diagnosis.

"And I went to all sorts of tests more or less every day. Blood tests, x-rays, EKGs, everything...but they didn't find anything". (P4)

Others, in retrospect, reflected that their GP too readily accepted the participant's lay rationalization of the symptom(s), i.e., being busy, not eating well. Others experienced that the GP initially misattributed symptoms to common ailments, for example stress, indigestion, or to an existing primary illness.

"When I look back my GP should have considered other explanations than those I came up with. Of course it could have been my COPD. I mean, I never suspected anything else and I didn't press for anyone to look for anything else." (P1).

Those encountering a "thinking out of the box" approach described that they were referred to further testing by the GP as "at suspicion of cancer." This entailed fast-track diagnostic testing according to current national guidelines. Participants presenting with jaundice were overall referred immediately to fast track diagnostic testing. Among those who experienced their symptom(s) were initially "put on hold" for further observation or misattributed to more "innocent" diseases, some described the subsequent journey to diagnosis as prolonged and tedious. They described a feeling of being pawns in the diagnostic process, because they were thrown back and forth between specialties and health care sectors. They were angry and concerned that the time spent waiting for the right diagnosis had compromised their chances of cure.

"They [the physicians] said we have to be sure that it isn't cancer and nothing points towards that. Well great - hurrah. But then when you get the result of the next test they say it might be cancer so you'll have to see the specialists at the specialist hospital. All the time - back and forth. You can't help question all this back and forth and ask yourself how much has the cancer grown meanwhile. We'll never get the answer to that, but that's why we've been angry." (P5).

Among participants with non-specific symptoms, some blamed themselves for having delayed the diagnosis, either by delaying help-seeking or initially preferring to accept apparently "innocent" explanations rather than insisting on further testing.

Those experiencing swift referral experienced a sense of relief despite the fear associated with referral due to suspicion of cancer.

"For me all the waiting has been hard. As soon as you're in the system [the hospital] things start to happen and you get a new examination date every time and then waiting is bearable." (P7).

"Being in the know" during the journey to diagnosis

On the journey to diagnosis, participants described that a feeling of being well-informed or "in the know" invoked a sense of control. Concrete information, even when preliminary, enabled patients to understand and cope with the range of potential diagnoses considered during diagnostic testing. Concrete information demystified and facilitated understanding of the various tests they underwent, and creating a feeling of trust and control on the diagnostic journey. Some participants described how they explicitly asked for straightforward information en route to diagnosis.

"So I sat down and said give it to me - meaning I don't want anything to be withheld or wrapped up". (P9).

"You don't have any clots in your lungs, but you should be prepared for the worst. The she told me right out that I had cancer. For me it was good that she told me so directly. She didn't wrap anything up in a nice parcel - I mean that's the reality if things so now I just have to move on from here". (P15).

Opposed to this, the participants described the insecurity that arose from lacking information or information they felt was not factual but based on the individual clinician's subjective experience.

"He [the physician in the surgery unit] said to me that the cancer was slow-growing. How do you know that, I asked? Well it's my experience. At the oncological unit she [the physician] said to me the cancer is fast-growing. How can you say that, I asked? Well that's my experience." (P14).

Consistency in the information disclosed across specialties and from the clinicians they met on route to diagnosis was important. Participants stated that they did not have the surplus energy to cope with the insecurity of inconsistencies. Not only were inconsistencies confusing, they were also anxiety-provoking because participants became doubtful of what information to rely on. One participant for example described a situation in which the surgical and oncological specialties as well as physicians from within the same speciality told him four different things.

"I mean four different physicians told me four different things... If they had said the same things, I would have been much more at peace." (P4).

During diagnostic testing, the participants further sensed that clinicians assessed them individually to determine how comprehensively and bluntly they should disclose information. The participants experienced that disclosing positive information was uncomplicated for clinicians. However, if the news were bad, participants felt unsure if they were fully informed. They questioned whether the clinicians chose to disclose only the parts of the picture they determined the individual patient capable of hearing.

"If he [the physician] says you're cured, then you're cured. But if you're not cured, how much will he [the physician] say then? I mean if you're a physician or a nurse do you consider how much he can [the patient] take? How much of the truth do you [the patient] actually get to know?" (P5).

The feeling of being selectively and not fully informed concerned participants and introduced feelings of mistrust and loss of control.

Discussion

The aim of this study was to explore CCA patients' descriptions of initial symptoms of disease, help-seeking behaviour, and the journey to diagnosis.

Initial symptoms of disease were largely non-specific and vague. Specific symptoms included jaundice and to some extent weight loss. Specifically jaundice prompted immediate GP consultation. Non-specific symptoms were often normalized, for example explained away by stress, being busy etc., particularly in the absence of pain, or considered too undefined to justify help-seeking. When consulting their GP, some participants experienced a "thinking out of the box" approach to diagnosis, for the most part leading to swift referral for further testing. Others experienced that symptoms

were misattributed to common or existing ailments or the patient's own lay rationalisation of the symptom(s). Participants considered, in hindsight, that the latter approach combined with their own reluctance to consult their GP may have delayed diagnosis and worsened their prognosis. Concrete information, even if preliminary, reduced anxiety and facilitated a sense of trust and control on the journey to diagnosis.

Our findings indicate that patients delayed help-seeking behaviour when experiencing non-specific symptoms while reacting more promptly to specific symptoms such as jaundice, weight loss and pain. Normalising non-specific symptoms, finding them hard to explain or preferring to wait and see if they disappeared potentially delayed diagnosis.

Conversely, specific symptoms, particularly jaundice, triggered prompt help-seeking. Our findings correspond to the findings of a qualitative synthesis of patients' help-seeking behaviour and delays in cancer presentation [10] and to the experiences of patients diagnosed with cancer of unknown primary [24]. Lacking recognition and misinterpretation of illness symptoms and fear of embarrassment were major causes for delayed help-seeking [10]. Our findings point toward an ongoing need for public sanctioning of help-seeking behaviour so the apprehension to seek medical help for fear of embarrassment and fear of taking up the GP's time with "insignificant" symptoms is reduced. Bethune et al. for example found that an awareness campaign on bowel cancer, encouraging people to consult their GP with non-specific symptoms, in some cases reduced delays in diagnosis [25]. Campaigns promoting sanctioning of help-seeking could come from the health care sector, media and patient organisations.

Future studies could also examine the effect of targeted sanctioning of help-seeking for patients with known risk factors for CCA, for example people with primary sclerosing cholangitis, viral hepatitis and cirrhosis [2]. As family and friends appeared to facilitate participants' help-seeking behaviour similar to the findings of Fish et al. [26], public campaigns highlighting the importance of family and friends in encouraging help-seeking behaviour may also be relevant. Our findings suggest that patients with well-recognised specific symptoms (e.g. jaundice) and those experiencing GPs with a "thinking out of the box" approach to non-specific symptoms experienced a swifter diagnostic process potentially allowing for earlier diagnosis. However, in the perspective of some participants, health professionals in some cases contributed to delayed diagnosis by going along with the participants' normalisation or explaining away of symptoms. Studies show that existing comorbidity can sometimes accidentally lead to diagnosis of CCA [6,26]. Conversely, comorbidity may delay diagnosis if new non-specific symptoms are misattributed to benign diagnoses or if non-specific symptoms in young patients fail to raise GP suspicion [27].

Normalisation and downplaying of symptoms by patients may delay help-seeking and potentially diagnosis. The challenge facing GPs is how to uncover normalised symptoms hidden in everyday explanations from patients. Brindle et al. suggest that for GPs to get to such hidden symptoms, they

need to ask close-ended questions that do not allude to disease-related symptom labels [28]. This differs from the exploration of symptoms perceived as abnormal by patients through open-ended questions. Regular GP consultations targeting those with known risk factors for CCA with the specific aim of eliciting health changes that appear harmless or are otherwise normalised by patients could be an approach [28]. Early detection of CCA is however extremely challenging given that two-thirds of CCA remain clinically silent and the remaining cases largely present with non-specific symptoms despite advanced disease [29].

Concrete information, even when preliminary, throughout the journey to diagnosis was important for participants whereas inconsistent and selective disclosure of information led to insecurity and mistrust. In the present study, participants particularly experienced that it appeared difficult for clinicians to tell the truth when the truth entailed bad news. Similar findings are identified in a synthesis of qualitative studies of information-seeking behaviour in patients with different cancer sites [30]. Insufficient information and collaboration between health services was likewise reported by patients in a survey of Danish cancer patients. Fourteen percent of patients experienced inconsistent information between hospitals, and 20% insufficient collaboration between GPs and hospitals [31].

The disclosure of information by clinicians appears dependent on many factors: the dynamics of the individual interaction between clinicians and patient, institutional and professional norms, the degree of training in conveying bad news, and exposure to the wishes of family in regard to disclosure [32]. Undoubtedly, clinicians need a significant level of communication skills, emotional capability, training and experience to be able to convey bad news [33,34]. Positive attitudes to disclosure of information to patients should be encouraged through professional and institutional norms and education in breaking bad news and addressing emotional responses to bad news [30].

It is furthermore important to be aware that the informational needs of patients may evolve over time during the journey to diagnosis and through treatment. Germini et al. [35] are currently exploring this in a prospective, longitudinal qualitative study. The aim is to gain insight into how information-seeking behaviour in cancer patients may change across different stages of the patient journey and the subsequent consequences of potential changes for clinical practice [35].

Rousseau et al. [36] suggest that patient navigation could address informational and communication needs of patients. Patient navigators may potentially play a pivotal role both en route to diagnosis and throughout treatment by ensuring that individual needs for information are met, thereby allowing patients to experience control of their situation [38,39]. According to Clark et al. [37] patient navigators currently mainly offer direct practical help and physically escort patients through the health care system. CCA patients might benefit from systematic patient navigation focusing not only on

practical help but also on ensuring individual wishes for information during diagnosis and treatment.

Studies report that uncertainties persist long after initial treatment in cancer patients and their partners [39]. Our results suggest that uncertainties may be even more severe in patients experiencing a prolonged and complicated diagnostic trajectory. This has important implications for clinicians who need to tailor treatment and care accordingly [40].

Trustworthiness

The trustworthiness of the findings should be considered in terms of their credibility, transferability, dependability and confirmability [41,42]. To achieve credibility, interviews took place at home or at the referral centre, as preferred by participants. To enhance credibility, the interviewer constantly checked her understanding of participants' experiences during interviews [43].

Three authors with different clinical backgrounds and distance to the research topic analysed data. This blend of perspectives and distance contributes to the credibility and dependability of the findings. We further strived to sample participants strategically to achieve variations according to age and gender. Confirmability was furthermore sought obtained in the interaction between the presentation of findings and the quotations illustrating them.

Limitations

Placing interviews in connection with chemotherapy treatment or scheduled follow-up consultations might have influenced participants, for example to be more critical or less active, if they were nervous before treatment or felt unwell and tired after treatment. Participants had previously met one of the investigators. This might have increased their trust and enabled them to be more open during interviews. However, it might also have caused them to be less open, specifically less overtly critical if they feared this could affect their treatment negatively. Due to rapid disease progression, 8 patients were unable to participate in interviews. This is a potential limitation of the study given that they may have contributed additional, valuable data.

Conclusion

To the best of our knowledge this is the first study that qualitatively explores CCA patients' descriptions of early symptoms of disease, initial help-seeking behaviour, and the journey to diagnosis. Participant's initially experienced non-specific or specific symptoms, with the latter largely leading to immediate GP contact and referral to fast-track diagnostic testing. Conversely, participants tended to normalise and delay help-seeking behaviour when experiencing non-specific symptoms. Misattribution of non-specific symptoms likewise delayed diagnostic testing. This indicates a need for reinforcement of public awareness of the importance of reacting to non-specific symptoms. Moreover, health professionals face the challenge of uncovering non-specific

symptoms that are normalised or downplayed by patients. Concrete information, even when preliminary, throughout the journey to diagnosis was important for participants. We suggest that patient navigators could play an important role in ensuring that patients' information-seeking needs are addressed. Furthermore, clinicians should be mindful that participants who experience a prolonged diagnostic trajectory carry the uncertainties of this experience with them throughout treatment and when transitioning to survivorship.

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Disclosure of Interests

The authors report no conflicts of interests. We do not have a financial relationship with Flemming Topsøe in any way.

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