

RESEARCH ARTICLE

Living outliers: experiences, insights and narratives of exceptional survivors of incurable cancer

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ABSTRACT **Aim:** Unexplained prolonged survival given a diagnosis of incurable advanced cancer is a puzzling phenomenon that recently has attracted more scientific research. The purpose of this study was to add to the understanding of how exceptional patients perceive and explain their unusual experience. **Methods:** We recruited patients for interviews from a population registry, patients with advanced lung or pancreatic malignancy who experienced exceptional survival. **Results & conclusion:** In total, 15 participants were interviewed. The main recurrent themes in most of the interviews were patient–doctor communication, family support and the patient’s proactive attitude. In this study, patients attribute their longevity to relationships with their doctor and their family – not the type of treatment they received. Further research on this phenomenon is needed.

Exceptional disease course and spontaneous regression of cancer is a well-documented medical event [1–54]. Over the last five decades, several terms have been used to describe the phenomenon of exceptional patients with cancer: spontaneous remission, spontaneous healing, spontaneous regression [1], miracle cures [2], remarkable recovery [3,6], radical remission [4] or exceptional disease course [5]. The defining criteria of the exceptional patient are controversial. Gotay defined ‘an exceptional survivor as a cancer patient who is alive when the probability is less than 25% of living for 5 or more years, for a given type and stage’ [48].

The research that has examined these success stories has been limited and unable to provide a satisfactorily clear explanation. Research has focused on physiological factors, including immunological factors, the elimination of carcinogens or antigens, anti-angiogenesis and tumor necrosis, apoptosis, genetic and epigenetic mechanisms and possible psychological mechanisms [1]. Others note that a certain percentage of patients have undergone some kind of spiritual awakening before the remission, suggesting that the patients themselves had an important role in the healing process [16,44].

Much of the literature is based on individual case reports. Challis and Stam reviewed reported cases from 1900 to 1987 and estimated that approximately 20 cases a year are reported [45]. Jerry and Challis estimated that exceptional survival occurs not more than once in 60,000–100,000 patients with cancer, but the true incidence is unknown [46]. Some argue that exceptional disease course is only reported in the rare case, when regression is both dramatic and durable and that less dramatic courses tend to get overlooked and are almost never reported [47].

KEYWORDS

- alternative medicine
- cancer care
- cancer survival
- complementary medicine
- hope
- patient–doctor communication
- prognosis
- spontaneous neoplasm regression
- spontaneous remission

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In Norway, the National Research Center in complementary and alternative medicine (CAM) established an Exceptional Case History Register; so far, they have documented over 300 patients, 60 of whom are cancer patients [55]. Understanding this phenomenon and the possible mechanisms involved may have significant preventative and therapeutic implications.

Recently, researchers at the University of Texas MD Anderson Cancer Center, in collaboration with Israeli researchers [44,51], approached leading clinicians at two comprehensive cancer centers and identified 26 exceptional patients. After interviewing these patients, the researchers found several common themes: activism, open communication with physicians, support from family and friends and belief in a higher power [44,51].

Unfortunately, this study had some weaknesses. One of the weaknesses was that the sample size did not reflect the true occurrence of exceptional patients among the general population. Another weakness was related to the selection bias, as the patients were identified by their treating physicians.

The purpose of this study was to identify exceptional patients through a population registry as it reflects the true occurrence of this phenomenon. To overcome the obstacles we identified from earlier studies, we used a similar qualitative methodology in our study, but we identified exceptional patients through a computerized population registry system that is part of the Israeli healthcare system, which allowed us to identify the true occurrence of exceptional patients with specific cancer types that have a very poor prognosis. This registry accurately tracks patients' medical care, and patients cannot disappear from the system, even though they might not follow the conventional treatment trajectory, might change location or might change providers.

Methods

Our study used a qualitative approach consisting of in-depth, open-ended interviews. This approach, widely used in the context of healthcare, was deemed most appropriate to capture the perceptions and experiences of exceptional patients [6,44,48,49,51,53,54,56,57].

• Setting & participants

We recruited patients from Clalit Health Services, the largest health maintenance organization in

Israel, from one region with a total population of 630,000. The study was approved by the Clalit Institutional Review Board.

From 2012 to 2014, we used the registry to identify exceptional patients in whom advanced lung or pancreatic cancer was diagnosed between 1997 and 2008 and who survived over 5 years from the time of their diagnosis to the time of our study, despite a predicted 5-year survival rate of less than 15%. Each patient's physician was contacted to verify the diagnosis. An additional oncologist, external to the study, reviewed each patient's chart to verify the diagnosis and expected prognosis. Patients' physicians were asked to contact patients and obtain their consent to participate in the study.

Patients were excluded from the study if they did not consent, had medical conditions that would preclude participation in an interview session lasting over 30 min, or had a diagnosis of active psychosis or severe cognitive impairment.

We were aware that pancreatic cancer is heterogeneous group of diseases, so we included in our study only patients with adenocarcinoma of the pancreas which has a grim prognosis that fit our inclusion criteria, disease state with less than 15% 5-year survival, and all the other types of pancreatic malignancy such as neuroendocrine or mucinous cystadenocarcinoma were excluded.

• Interviews

We formulated structured interview questions to encourage participants to describe their experience of exceptional survival. The main question was open-ended: "Tell me about your experience of having an exceptional disease course." Patients were asked to elaborate on the way the experience changed their lives (if at all), their understanding of their prognosis, their lifestyle changes, their perceptions of exceptional survival, their use of CAM, their rationalization (if any) of their exceptional status and their explanation (if any) of behaviors or factors that caused their exceptional survival.

All interviews except two were conducted by one qualitative researcher (S Gross), who also led the analysis. Interviews lasted 30–90 min; all interviews except one were recorded and fully transcribed. The interviews were in Hebrew, except for two that were in Russian and that were translated into Hebrew.

The study end point was aimed at reaching saturation regarding the recurring themes that were extracted from the interviews [56,57].

• **Data analysis & interpretation**

Our qualitative content analysis used grounded theory methods focused on contextual meaning and the interpretation of narrative text [56,57]. Two experienced qualitative researchers independently examined the interview transcripts (S Gross and AP Giveon) and identified common categories, themes and subthemes for cross-validation. The analyses were done in the patients’ native language (13 in Hebrew and two in Russian).

Descriptive analysis of sociodemographic, disease-related and treatment-related factors was conducted to characterize the sample and to verify that sampling criteria were met.

Results

Twenty-three patients with advanced lung or pancreatic cancer were identified through the regional computerized registry. Eight of the patients were excluded from the study owing to incorrect diagnosis (five), refusal to participate in the study (one) or severe cognitive impairment (two). In total, 15 participants agreed to be interviewed (nine women and six men). All patients were in remission with regular follow-up. Eight of the patients had advanced lung cancer and seven had pancreatic adenocarcinoma (Table 1). The mean survival duration since diagnosis was 8.2 years (range: 5–15 years) with patient’s average age of 70 years. All the patients received conventional treatment, including surgery, chemotherapy and radiation therapy. At time of

interview, all the patients had ECOG performance status of 0–2 and were able to participate in the interviews that lasted 30–90 min.

• **Perception of survival**

Many of the patients could not see themselves as either past the disease or cured. For many of these patients, who still suffer from symptoms of cancer and from deterioration in their functioning, the definition of survivorship can only be understood literally: that is, not having perished, but certainly not in terms of having won the battle with the disease. However, most of the patients were elderly, making it difficult to disentangle the effects of the disease and of age on their functioning. We expected patients to be excited about the new life they were given; however, we found that many patients felt that they had been shattered by the prognosis and that ‘over-surviving’ made even less sense than the disease itself and was therefore more distressing.

This seemed to be the case for P2, a 57-year-old woman who suffered from considerable neck pain (resulting from bone metastases of lung cancer) and was unable to move her head in all directions. She equated the disease to a hump on one’s back: “you can’t take it off. It’s here.” Both P2 and her husband, however, still emphasized her survival beyond expectations, and though prepared for her death, they said they found her death more remote than they could have dreamed. It seemed as though they were stretching their arms toward her death, which

Table 1. Demographics and diagnosis data for cancer patients who survived despite a 15% 5-year survival rate.

Patient number	M/F	Age	Dx	Dx date	Date of last consultation
1	F	79	Pancreatic cancer	2007	November 2012
2	F	57	Advanced NSCLC	2007	December 2012
3	F	83	Pancreatic cancer	1997	October 2012
4	M	81	Pancreatic cancer	2005	2012
5	F	65	Advanced NSCLC	2004	October 2012
6	F	73	Advanced NSCLC	2002	November 2012
7	M	75	Advanced NSCLC	2004	September 2012
8	F	76	Pancreatic cancer	1997	October 2012
9	F	59	Advanced NSCLC	2006	November 2012
10	F	77	Advanced NSCLC	1999	October 2012
11	M	61	Advanced NSCLC	2007	March 2013
12	F	75	Pancreatic cancer	2005	April 2013
13	M	61	Pancreatic cancer	2007	March 2013
14	M	67	Pancreatic cancer	1997	October 2012
15	M	65	Advanced NSCLC	2002	March 2013

Dx: Diagnosis; F: Female; M: Male; NSCLC: Non-small cell lung cancer.

kept slipping farther away, dwindling both their emotional and financial resources.

P1 seemed tired and resigned to her fate: “I now see that I have lived with that cancer for 16 years ... But I won’t live 16 more years; I couldn’t even if I wanted to ... I’m at that age where it’s enough. You can’t live to be a 100 years.”

Two-thirds of the patients ($n = 10$) looked forward to seeing their children/grandchildren marry, and these patients defined their will to live in terms of family events (births, marriages and Bar Mitzvahs among others). Only a minority (five) spoke of other aspects that made life worth living: enjoying the sun and the flowers, walking in the wilderness of the mountains, going to the beach and traveling abroad. P11 looked forward to his life with a woman he met just before he got sick.

Only about half of the patients spoke of regaining an appreciation of life as a result of the disease. P3 talked of her love of dancing. P14 said, “Of course now I appreciate life more.” P4 was grateful for the gift of new life (although this attitude may be related to his religious belief system). P11 said he used to be somewhat of a brooder, but now, after the disease, he wants to go out, to work, to see the world. P12 was grateful to be able to “get up every morning and praise the lord.” P13 said that every day is “a gift from heaven” and that she enjoyed each and every day.

• Themes related to survival

The main themes in the interviews that were related to extended survival were a unique patient–doctor relationship, family support and proactive attitude.

The patient–doctor relationship

The most prominent theme was the patient–doctor relationship. The typical account of the course of disease emphasized the roles of the ‘bad’ (or vilified) physician and the ‘good’ (or idealized) physician. The ‘bad’ physicians of these accounts lacked the proper vision to diagnose the disease accurately and treated patients rudely, dismissively, arrogantly or disrespectfully. The ‘good’ physician was portrayed as a savior: omniscient, omnipotent, benevolent, engaged, sensitive and decisive.

P2 described her doctor as an ‘angel’ and another as ‘amazing’ (specifically for not being aggressive in terms of treatment choices and for having a special type of intuition, knowledge

and experience). Another doctor was ‘first league,’ in that he was warm and caring. She contrasts these ‘good’ doctors with a ‘bad’ doctor who charged unreasonable sums of money for ‘10 min’ of consultation. He put P2 and her husband under a lot of stress: “She wasn’t even given a chance,” her husband said. “6 years ago, we were sure she would be dead in a month.” Because of her poor prognosis, her doctor advised against chemotherapy (deemed futile). When they eventually agreed to treat her, she was mentally exhausted because she had to fight so hard to be treated. For P2 and her husband, the physician’s attitude was more important than the treatment itself.

P3 had her own exceptional, ‘out of this world’ doctor. She described the surgeon who treated her as an ‘angel’ with “hands of an angel.” She mentioned the way he treated her: he brought her coffee (prepared exactly in the way her late husband used to make her coffee), and her doctor sat next to her bed, reassured her and wet her lips. This doctor was the only one she trusted; he was “more than a father, more than a brother.”

Family support

Family support was one of the strongest themes in our study; all but two patients referred to this component in their stories. Family support took diverse forms: from a broad consideration of several members of the family to a tendency to focus on one particular person, such as a son who happened to be a physician or a sister who happened to be a nurse.

Family members boosted morale, helped financially, helped with logistics (e.g., driving to the hospital), provided professional advice (when a family member was a physician or a nurse) and used connections to further care (when a family member knew someone in a key position).

It was often impossible to disentangle the story of the individual and the path he/she had taken from the role the family members played in the patient’s care. P1’s granddaughter lived with her. Yet, help at a more professional level came from P1’s daughter, a nurse who worked at a major hospital. P1 chose to undergo all treatments at the hospital where her daughter worked even though there were several hospitals nearer to her home.

P2 and her husband were in complete agreement in terms of explaining her remarkable survival. Both P2 and her husband agreed that she

would have died long ago without the help of her husband.

P4 also had a very supportive network of family and friends. P4 said, “When someone visits a sick person, he/she takes with him/her half of the sickness.”

Proactive attitude

A proactive attitude manifested in several ways in the patients’ narratives: getting second opinions, asking for advice from lay people such as friends, neighbors and family, turning to the private sector, going abroad, changing doctors, putting pressure on doctors to get more tests and further the diagnosis and, at times, openly questioning the diagnosis.

P1 definitely ascribed her survival to the fact that she asserted herself (with the help of her daughter) when turning to healthcare. She believed her decision to pursue private care and her unwillingness to give up may have allowed her to survive while her husband died 1.5 years after his cancer diagnosis. He had been more accepting of the system. P1 was quite proactive and demanded to be tested when she felt a need for it. It was her idea to undergo the computed tomography scan that allowed her doctors to identify a problem in her pancreas. She decided to go to a private clinic, when she felt public services were less adequate.

Many of the patients mentioned that ‘fighting the system’ was important for their recovery, but they usually spoke of other factors that were more important. Three patients (P1, P3 and P10) mentioned that ‘fighting the system’ was the main contributor to their remarkable survival. For example, P3 was repeatedly thrown out of the doctor’s office because of her tendency to ‘make scenes’. She took pride in her daring to scream for care at nights when she was hospitalized.

Use of complementary & alternative medicine

Most patients used different types of CAM; however, these patients generally did not think that CAM had much effect on their exceptional survival, and they did not find much sense in making lifestyle changes.

Several patients altered their diets but did not ascribe their recovery to these changes. P1 did not assign much importance to her diet of carrots, papaya, yellow vegetables, cinnamon and a plant (she could not translate the name from Russian), and she only mentioned her diet when

she was asked explicitly about CAM or natural medicine.

Some patients used supplements. P7’s daughter advised him to try *Astragalus membranaceus*, which he took. He decided not to try CAM, not because he believed it ineffective but because he was concerned that CAM might interact with his chemotherapy and cause harm. P5 went to see a physician-homeopath in The Netherlands and received pills from him. She remained skeptical about the role the pills played in her recovery. She said that the trip to The Netherlands helped her stop feeling ‘down’, but this was a matter of tourism and not of homeopathy. P14 opted for an algae treatment at a nearby hospital and thought this supplement helped strengthen him and helped with the nausea associated with chemotherapy.

P8 did guided imagery, until the instructor insisted that she should quit chemotherapy. She stopped going to the sessions but continued to use the method independently as she found some benefit in using it. When she had trouble sleeping, she tried Reiki but has since taken sleeping pills. She said that when she felt better she would try acupuncture.

Two patients participated in tarot card readings. P5’s husband went to see a professional tarot reader who read – accurately, it turned out – that a month later she had be healthy. She said, “Even now, I’m telling you, I don’t believe in it, but it’s a fact: He said so, and it happened.” P6 also went to see a tarot reader and was told that she should ‘accumulate’ words of wisdom, motivational phrases etc. She followed this advice and even sent herself flowers with a thank you note, to cheer herself up. She showed it to the researcher with great pride.

Two patients sought help from spiritual healers. P14’s daughter went to see a rabbi healer, who prescribed fish oil, vitamins, almonds, nuts and a sort of black powder from The Netherlands, which P14 would boil in water and drink twice a day; the rabbi healer also suggested not eating green food. P14 seemed skeptical about the healer’s suggestions, but he said that, at the time, he would have taken anything that anyone recommended.

P15 read books written by Ibn Sina, a traditional Islamic healer, to find advice on herbal medicine. He treated fungus on the palms of his hands with mucus from snails in his backyard, but he did not use CAM for anything cancer-related.

Discussion

We recruited exceptional patients through an objective population registry that accurately reflects the occurrence of exceptional patients among the general population. In a period of 11 years, we found 15 exceptional patients with advanced lung or pancreatic cancer and an expected 5-year survival rate of less than 15%.

All patients with cancer who survive beyond their life expectancy are, by definition, outliers and defy our understanding of the nature of cancer. Yet, when we learn more about the lives of these survivors and the nature of their survival, we may question the narrow definition of exceptionality that is based on lifespan rather than on quality of life. In this case, it seems, more can be learned about not only their remission (which may not have been achieved) but also the meanings they attach to their exceptionality, whether expressed in mere lifespan or in full functional recovery. Although poor quality of life caused several patients in our study to perceive their survival as distressing, half of the patients did regain an appreciation of life as a result of the disease.

Although our study used a population registry to identify exceptional patients, our results are similar to those of the MD Anderson study [44,51]. The interviews from the two studies show different patterns but share several themes: the patient–doctor relationship, family support and the patient’s proactive attitude.

In our study, the role of the physician in the patient–doctor relationship was much more emphasized than in the MD Anderson study. Many patients related their unique survival to an exceptional physician. The typical narrative in our results describes a vilified, incompetent physician and a savior physician. This issue was also discussed in the MD Anderson study [44,51], which emphasized the importance of communication patterns: the physician’s compassion, demeanor, availability, honesty and sensitivity in the decision-making process were emphasized. Most of our patients also thought the patient–doctor relationship was the critical component of their healing. After patients being ‘thrown’ between many physicians, being helpless and lacking understanding and knowledge about the disease and treatment options our patients described meeting an exceptional physician who was able to help. These doctors could think ‘out of the box’, and our patients believed that these exceptional doctors snatched them from death.

Both studies also emphasized family support as a major factor in survival. In the MD Anderson study, participants articulated the importance of connections with family and friends as a major factor in dealing with their illness [44]. In our study, however, patients emphasized family support more than friend support.

A proactive attitude was also a recurrent theme in both studies, though much more emphasized in the MD Anderson study. All the narratives obtained in that study had some form of activism, manifesting in the conscious decision either to continue with everyday life or to change one’s life as a means of avoiding passive submission to the disease. Our patients also mentioned that being proactive in their treatment was important for their survival. A proactive attitude was exemplified by patients who asked for second opinions from professionals and others, questioned the diagnosis, changed doctors and insisted on being involved in the diagnostic process and treatment decisions.

In our study, although most patients mentioned the use of CAM, none of the patients ascribed their exceptional survival to CAM. Some methods may have helped not with the cancer itself but with related side effects of conventional treatment, such as nausea and weakness.

Although we designed the study to include exceptional patients who may have dropped out of the healthcare system, we did not find any patients outside of the healthcare system. All patients in the study received conventional treatment; they might have changed providers or location, but, in Israel’s current healthcare system, patients cannot disappear from surveillance owing to refusing recommended treatments or using unconventional treatments or alternative therapies not recommended by their healthcare providers. In Israel, all citizens have state healthcare coverage, which is closely monitored by four health maintenance organizations that report to the Ministry of Health, so patients cannot drop out of the system unless they immigrate to another country.

This study has some weaknesses because of its qualitative design and because we obtained subjective information and perceptions from patients. On the other hand, a qualitative approach is deemed most appropriate to capture the perceptions and experiences of exceptional patients. This research method allows participants to describe an experience in the way that is most meaningful to them. This approach

has been widely used in the healthcare system to better understand patients' perspectives and experiences [56,57].

The study had a small number of participants, but our results did reach saturation regarding the recurring themes that were extracted, an end point that is commonly needed in qualitative research [56,57].

The information obtained in this study can be used to increase awareness to the issue of exceptional patients in cancer care even when odds are slim for survival. This information is not just important to increase hope in both, physicians as well as patients, but also helpful for developing future research projects in cancer care and survivorship.

The lessons learned can lead to additional studies that incorporate these issues such as patient–doctor communication, the value of being proactive in care as well as the other points mentioned.

Many questions still need to be explored to understand why some patients survive despite a dismal prognosis. Unfortunately, the USA does not have a national exceptional disease course registry to track unexplained cases. Such a registry would be an invaluable resource for studying the causes of exceptional survival.

Conclusion

Utilizing a population registry reveals only a small number of exceptional patients, cancer

EXECUTIVE SUMMARY

Background

- We define exceptional patients as cancer survivors who became disease-free or experienced unexplained prolonged survival given a diagnosis of incurable advanced cancer.
- This exceptional survival is a puzzling phenomenon that recently has attracted more scientific research.
- The purpose of this study was to add to the understanding of how exceptional patients perceive and explain their unusual experience.

Methods

- The study used an exploratory qualitative approach consisting of in-depth, semistructured interviews with exceptional patients.
- We used a computerized population registry to identify patients in one region in Israel with a population of 600,000.
- We recruited patients with advanced lung or pancreatic malignancy diagnosed between 1997 and 2008 who experienced exceptional survival despite an expected 5-year survival rate of less than 15%.
- Patients were then contacted and interviewed; each conversation was recorded and then transcribed.
- Analyses followed validated techniques for qualitative content.

Results

- Fifteen participants were interviewed.
- The main recurrent themes in most of the interviews were patient–doctor communication, family support and the patient's proactive attitude.
- Having a caring physician was the leading theme among the patients that were interviewed.
- Even though most patients used some form of complementary and alternative medicine, they did not consider alternative medicine to be a main cause for their survival.

Conclusion

- In this study, we found that patient–doctor communication, family support and a proactive attitude were major themes in how exceptional patients explain their remarkable survival.
- Further research is needed to determine the true frequency of exceptional patients, the types of cancer these patients have, the characteristics these exceptional patients might share.
- An accurate database of exceptional patients may also provide another source of hope for patients and their families.

patients that exceeded all odds of survival. This distinctive group of cancer patients explains their extended survival to unique patient–doctor communication, family support and a proactive attitude. Further research on this phenomenon is needed.

Future perspective

Further research is needed to determine the true frequency of exceptional patients, the types of cancer these patients have, the characteristics these exceptional patients might share, the specific treatments used to manage these patients' care and other factors that might explain this phenomenon. More research is also needed to study patients who are from other locations, who were treated at other institutions and who have other types of cancer.

It would be helpful to develop a registry or database of these patients to record qualitative assessments of their experience [2–6,49,51,55]. An accurate database of exceptional patients may also provide another source of hope for patients and their families.

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Ethical conduct of research

The authors state that they have obtained appropriate institutional review board approval or have followed the principles outlined in the Declaration of Helsinki for all human or animal experimental investigations. In addition, for investigations involving human subjects, informed consent has been obtained from the participants involved.

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