Advance Care Planning in brain tumour survivors: a prospective study

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Abstract

Purpose: Advance care planning (ACP) is the process of planning for future healthcare to guide clinical decision making when one is unable to communicate decisions due to lack of capacity. This study explored the perspectives of brain tumour (BT) patients in discussing ACP, symptom profile, physical and functional status, quality of life (QoL), level of coping and carer burden.

Methods: A prospective cohort study with semi-structured interviews regarding ACP for BT patients in hospital and community. Validated assessment tools measured coping strategies, QoL and carer burden. Interview ACP transcripts were analyzed, coded and interpreted using qualitative analytic techniques for thematic analyses.

Results: Participants' (n=36) mean age was 47 years (range 20-69 years), with median time since diagnosis of 3.9 years and majority (70%) had glioblastoma multiforme (GBM). Fatigue was the most common symptom reported by 89% participants, followed by pain (53%) and cognitive impairment (39%). Overall, participants indicated good QoL and used more problem-focused coping strategies including 'acceptance' and 'positive reframing'. There was a 'moderate' level of carer burden. Thematic analyses indicated participants had limited understanding of ACP, and lack of such discussions with healthcare professionals. Majority preferred dedicated sessions by trained healthcare professionals especially medical staff.

Conclusion: The low uptake of ACP amongst BT patients' highlights need for increased awareness of ACP in clinical practice as it has an important role in enhancing patient autonomy and delivery of quality end-of-life care. The neuropalliative-rehabilitation model of care integrates care with treating teams and can provide timely ACP information to BT patients, with the need for multifaceted system-wide interventions in implementing ACP.

Keywords: Advance care planning, Brain tumour, Glioblastoma, Qualitative research

List of abbreviations
ACP: Advance care planning
BT: brain tumour
QoL: quality of life
GBM: glioblastoma multiforme
EOL: end-of-life
MEPOA: Medical Enduring Power of Attorney
AD: Advance Directive

Background
Primary brain tumours (BT) are a heterogeneous group of benign and malignant tumours arising from the brain parenchyma and its surrounding structures. The overall pooled incidence rate of primary BT is approximately 10.8 per 100,000 person-years [1]. In Australia, there are over 1200 deaths from benign and malignant BT annually [2]. Primary BT are predominantly malignant gliomas, and half of these are glioblastoma multiforme (GBM). Despite advances in available therapies, GBM patients have a short median survival of approximately 14 months [3]. BT patients often experience high symptom burden (including fatigue, pain and seizures), difficulties with mobility and self-care, cognitive and intellectual decline, behavioural dysfunction, and psychosocial issues. Further, aggressive treatment regimens can be associated with considerable adverse effects and psychosocial implications. There is a significant impact of these disabilities and cumulative BT-related issues on cancer survivors, their families and carers, as well as vocational issues, financial strain and reduced quality of life (QoL) [4,5]. Future uncertainty is a significant contributor to poor QoL.

Advance care planning (ACP) is the process which involves decisions made by patients, in consultation with substitute decision-makers, family and health care providers regarding their values, beliefs, goals of care, life sustaining treatment preferences and palliative care options, should they later become incapable of expressing these wishes [6]. ACP documentation can take many forms, and in the state of Victoria, Australia, may include Medical Enduring Power of Attorney (MEPOA), Statement of Choices form, Refusal of Treatment Certificate and/or Advance Directive (AD) [7]. Due to the dramatic change in life expectancy, limited effective treatment options and progressive neurological deterioration of BT patients, earlier ACP discussions are important in guiding end-of-life (EOL) care of these patients.

ACP is increasingly recognized as an important element in improving EOL care in Australia and internationally, as it allows patients to engage in an effective shared decision-making process with their clinicians, and increases patient and family satisfaction with EOL care [6,7,8]. Additionally, ACP has been shown to increase the likelihood of a person dying in his or her preferred place, increases hospice use, and reduces hospitalization rates [6,9]. Timely discussions of ACP also result in enhanced QoL for the patient, with lower stress levels, anxiety and depression in surviving relatives [6,9]. Although ACP is recognized as integral to quality care, particularly in cancer patients, it remains poorly integrated in routine care. The neuropalliative-rehabilitation model of care helps to address this gap by highlighting the similar roles provided by rehabilitation and palliative care teams involved in BT patients' care [10]. The role of the rehabilitation team in the BT cohort, similar to palliative care, is often aimed at reducing symptom burden, improving activity limitations and QoL with psychosocial support, and plays a supportive role in being able to deliver ACP information and facilitate ACP conversations.

ACP discussions are especially important in BT patients due to the rapidity of cognitive decline secondary to tumour growth, tumour-related seizures or treatment effects [11]. Other problems are also common in BT patients including delirium, dysarthria, dysphasia and personality changes, which lead to impaired communication and hampered discussions about complex EOL topics [12,13]. Additional known barriers to ACP conversations include patients' limited understanding of treatment options, and prognostic uncertainty. Many clinicians often avoid the topic in practice due to time pressures, insufficient communication skills training and uncertainty regarding timing of initiation and content of ACP with fear of destroying hope in patients [14,15]. System-related barriers include documentation policies, financial reimbursement, limited resources, fragmentation of care and legislative differences. Studies have indicated that only 10-45% of high grade glioma patients had an AD during their last three months before death [16]. In many situations, due to progressive neurological deficits and loss of consciousness of the patients in the later stage, often some of these decisions had to be made by family members, which may cause great distress, or their clinicians on their behalf.

ACP has been widely explored in the literature in different patient cohorts, including cancer, chronic renal failure, heart failure, chronic obstructive pulmonary disease and other life-limiting conditions. Several studies had previously investigated ACP in BT cohort [17,18,19]. Although the body of research in this area is growing, a recent systematic review highlighted sparse literature and lack of high quality studies examining ACP in BT patients, with heterogeneity amongst studies and their findings [20]. Our previous pilot feasibility study in a tertiary hospital in Australia had demonstrated limited awareness and experience of ACP in BT patients, highlighting gaps in the provision of ACP discussions in a tertiary centre [19]. This study extends on the findings of the previous pilot study. The aim of the study is to further examine BT patients' experience with ACP and to explore factors impacting their decision making on ACP, using both qualitative and quantitative methods. It is envisaged that the findings will improve system-wide practices and processes of ACP.

Methods
Participants and setting
This study was conducted in the Royal Melbourne Hospital (RMH), a tertiary facility in Victoria, Australia and was approved by the Human Research and Ethics Committee (HREC 2014.221). Participants were recruited from the neurosurgery database between February 2015-May 2017. A total of 37 patients were identified as eligible based on the inclusion criteria (described below), however, 1 patient declined to participate for personal reasons. Hence, 36 consecutive patients were recruited following completion of treatment including surgery, chemotherapy or radiotherapy. All study participants had a confirmed diagnosis of BT (ranging from WHO Grade I - IV) with the ICD Code (C71) for primary BT (main diagnosis) incorporating all 10 sub-codes that localize the brain tumour (C71.0- 71.9) or metastatic BT, and were at different stages across their illness trajectory with varying levels of physical and functional needs.

Inclusion criteria included: aged 18 years and above, with confirmed diagnosis of WHO Grade 1-IV or metastatic BT types made by relevant specialists, residing in Victoria, able and willing to give informed consent, medically stable, without severe cognitive impairment (MMSE≥22) and living within a feasible distance (60km radius from the hospital) for home interviews. Those with severe cognitive impairment (MMSE < 22) and who could not adequately communicate in English were excluded.

Procedure
An invitation letter was mailed to all potentially eligible. Those who responded were contacted by the primary researcher (KS) by phone to further explain the study rationale and objectives. Those who provided written informed consent were recruited for the study. Participants were aware that they could withdraw from the study at any time without having reason for doing so.

The primary researcher conducted ACP discussions and assessments using validated measurements tools (See measurement section) utilizing face-to-face interviews. Participants were interviewed at a venue of their choice (home or hospital). All inpatient participants' interviews were performed at a time most convenient for them in a private ward office. Each interview took approximately 1.5 hours. Participants were given rest breaks and assistance (if required) to complete the questionnaires, but were not prompted.

All interviews were audiotaped, transcribed, anonymously labelled with a study code by the primary researcher and information was stored in a locked office at the RMH. Information was entered into a password protected database once all information had been collected. Study patient numbers were determined when data saturation point was reached; this describes a point beyond which

no new concepts arose as a result of further interviews [21].

Measurement & Questionnaires
Each participant was interviewed using a structured format and the following information was collected.

Brain tumor related information
This included socio-demographic data and clinical/medical data (co-morbid conditions, BT-related symptoms, tumour type and grade; and treatments received: surgery; chemotherapy). Further, their mobility and functional status were recorded.

Quality of life and coping measures
The McGill Quality of Life (MQOL), a valid and reliable measure, was used to assess participants' QoL [22]. It is a 16-item questionnaire with each question rated from 0 (not at all) to 10 (extremely). This questionnaire has previously been used in ACP studies [23]. The MQOL five domains include: 2 health related (physical well-being, physical symptoms) and 3 non-health related (existential wellbeing, psychological symptoms and support). For each domain, the score was the mean of values of the relative items. A total score was obtained adding up mean values of the score of the five domains. In addition, the participants were asked to indicate his/her perceived QoL in the past two days in a single item scale (MQOL-SIS), rated from 0 (very bad) to 10 (excellent).

The BRIEF-COPE inventory assessed participants' effective and ineffective coping capabilities. It has 14 subscales including active coping, planning, positive reframing, acceptance, humour, religion, using emotional support, using instrumental support, self-distraction, denial, venting, substance use, behavioural disengagement and self-blame [24]. Each subscale has 2 items.

Caregiver stress and burden
Caregiver stress was examined using the self-rated burden (SRB) scale [25]. The SRB is a single rating scale scored in millimetres along a 10cm line, with score range between 0-100. Caregivers are asked to indicate on the scale "how burdensome do you feel caring for your partner is at the moment". "0" will indicate no strain at all, and "100" will indicate much too strain. A higher score correlates with higher subjective burden. This scale has been found to be a feasible and valid measure of subjective burden amongst caregivers of stroke patients [26].

ACP discussion
After rapport had been established with the participant, interviews were then conducted with participants regarding ACP using initial open-ended questions followed by semi-structured pre-formatted interview questions to aid fluency of discussions. Flexibility was allowed to follow new lines that evolved during the discussion. Patients were also informed of the option to be referred for supportive counselling should they experience any significant distress.

Data analysis
A series of descriptive analyses were conducted on patient demographics and disease characteristics data. Additional analyses were conducted on the subscale scores of the MQOL, BRIEF-COPE and carer SRB, and presented in a descriptive manner. A series of analyses were conducted to describe the current status of wellbeing, coping capabilities and QoL of participants and to identify those factors associated with scores on these scales. Continuous predictor variables (age, time since diagnosis) were split at the median to form approximately equal groups for comparison. Parametric analyses (T-tests, ANOVA) were used to compare scores across groups. Although a substantial number of univariate analyses were conducted, increasing the likelihood of a Type 1 error, it was decided to report all p values above 0.05 as significant. This was consistent with the descriptive nature of the study to ensure all potentially important predictors of the current status of BT were identified. All data was entered twice to avoid errors on data entry. Statistical Package for Social Sciences (SPSS), v. 18.0 (SPSS Inc, Chicago, IL) was used for all analyses.

Interview transcripts regarding ACP discussions with the participants were analyzed, coded and interpreted using thematic analysis, guided by the analytic hierarchy [26]. Thematic analysis was based on an inductive process that allowed for themes to emerge, and to enable management of large amounts of qualitative data in a credible and robust manner [26]. Transcripts were individually read, 'open' coded, and emergent thematic features were collectively discussed, categorized and summarized under each topic domain by 2 investigators (KS, FK). This summary was then further summarized and certain points re-categorized as appropriate until agreement was reached. When no new themes were found, data saturation was considered to be achieved.

Results
Sample characteristics
The socio-demographic and clinical characteristics of study participants are presented in Table 1. The mean age of the participants (n = 36) was 47 years (Standard deviation (SD): 13.5, range 20-69 years), half were female (n = 18, 50%) and more than half were Caucasian (67%). Average time since BT diagnosis was 3.9 years (SD: 3.4, range 0.2-14.3 years). The majority of the participants (69%) had GBM and 3 participants had metastatic BT. All except two had surgery and 81% had radiotherapy. Patients were at different stages across the illness trajectory at time of interview, with half of the sample (n=18, 50%) requiring assistance for activities of daily living, and 9 participants (25%) requiring assistance for mobility.

Current symptoms
Fatigue was the most common symptom reported by the participants (88.9%), followed by pain/headache (52.8%), cognitive impairment (38.9%), and visual impairment (diplopia) (33.3%). Almost half of participants reported anxiety (47.2%), while depression was reported by 16 participants (44.4%). All participants' cognition appeared grossly intact during the interviews, with MMSE scores ranging from 27-30.

Table 1: Socio-demographic and clinical characteristics of participants (n = 36)

Characteristics		n, (%) (unless stated different)
Age (Mean ± SD (range) years	47.1 ± 13.5	(20-69)
Sex - Female	18	(50.0)
Marital status - Married/Partner	27	(25.0)
Living arrangements - Family	32	(88.9)
Education		
Secondary	24	(66.7)
Tertiary/Postgraduate	12	(33.4)
Ethnicity - Caucasian	24	(66.7)
Religion		
Christian	6	(16.7)
Other	30	(83.3)
Brain tumour type		
Meningioma	8	(22.2)
GBM	25	(69.4)
Metastatic	3	(8.3)
Time since diagnosis (Mean ± SD (range) years	3.9± 3.4	(0.2, 14.3)
Setting - Outpatient	28	(77.8)
Treatments		
Chemotherapy	23	(63.9)
Radiotherapy	29	(80.6)
Surgery	34	(94.4)
Comorbidities		
Diabetes	1	(2.8)
Hypertension	5	(13.9)
Hypercholesterolemia	3	(8.4)
Depression	16	(44.4)
Anxiety	17	(47.2)
Other (gout, arthritis, asthma)	9	(25.0)
Main symptoms		
Fatigue	32	(88.9)
Headache/pain	19	(52.8)
Cognitive impairment	14	(38.9)
Visual impairment (diplopia)	12	(33.3)
Seizures	8	(22.2)
Speech impairment	7	(19.4)
Assistance required for mobility	9	(25.0)
Assistance required for ADLs	18	(50.0)

ADLs = activities of daily living; GBM: glioblastoma; IQR= Inter quartile range; SD = standard deviation.

QoL & coping strategies

Overall, participants indicated good QoL (MQOL total mean: 97.3±16.8, SIS mean 6.6±1.7). The lowest mean scores (indicating greatest distress) in the MQOL for participants were on subscales for 'physical symptoms' (mean = 14.0±4.6, range = 6-28), 'existential well-being' (mean = 40.1±8.2) and psychological well-being' (mean = 28.5±8.7). Problem-focused coping strategies were more commonly used than emotion-focused coping strategies (BRIEF-COPE). Acceptance, active coping, using emotional support and positive reframing were the most commonly used problem-focused strategies by participants in the study (Table 2). Amongst the emotion-focused coping strategies, 'self-distraction' was the most commonly used strategy by the participants (Table 2).

Carer burden

The median score on the caregiver SRB scale was 57 (IQR 0, 90), which indicates moderate level of burden from demands of caregiving.

Table 2: Descriptive statistics for subscales of the of McGill Quality of Life (MQOL), and Brief-Cope (n = 36)

Measurement Scales	Mean (SD)	Range
MQOL		
Total	97.3 (16.8)	64-129
Single item scale (SIS)	6.6 (1.7)	3-10
Physical symptoms	14.0 (4.6)	6-28
Physical well-being	6.6 (2.3)	0-9
Psychological symptoms	28.5 (8.7)	10-40
Existential wellbeing	40.1 (8.2)	19-53
Support	14.8 (4.0)	6-20
BRIEF-COPE		
Problem focus coping strategies		
Active coping	6.5 (2.2)	2-8
Planning	6.1 (2.2)	2-8
Positive reframing	6.3 (1.8)	2-8
Acceptance	6.8 (1.4)	2-8
Humour	5.3 (2.7)	2-8
Religion	3.9 (2.3)	2-8
Using emotional support	6.8 (2.0)	2-8
Using instrumental support	5.8 (2.1)	2-8
Emotion-focused coping strategies		
Self-distraction	5.7 (1.7)	2-8
Denial	2.8 (1.3)	2-7
Venting	4.1 (2.1)	2-8
Substance use	2.1 (0.3)	2-4
Behavioural disengagement	2.4 (0.9)	2-6
Self-blame	2.9 (1.4)	2-7

Factors associated with current symptoms/impairments & other disease characteristics

A series of univariate analyses were conducted to identify predictive factors associated with current symptoms and impairments, as well as other disease characteristics, using the MQoL and BRIEF-COPE inventories. There were no statistically significant differences associated with gender for MQoL and BRIEF-COPE scores.

Scales scores for age group were compared by splitting the age into

two groups (≤49 and ≥50). The younger group showed statistically significant differences in three of the MQoL subscales (physical well-being, p=0.04; existential well-being, p=0.01; support, p=0.04) and two of the BRIEF-Cope (active coping, p=0.02; religion, p=0.05), indicating that younger participants tend to be physically well and coping better, as well as using religion as a coping strategy compared to their older counterparts. There were no significantly different scores across the tumour groups including meningioma, GBM or metastatic BT.

Time since diagnosis was split into two approximately equal groups (≤ 3 years and 3+ years). There were significantly different scores across these groups on two of BRIEF-COPE subscales (using emotional support, p=0.01; denial, p=0.03), indicating those recently diagnosed tends to use emotional support and denial as their coping strategies compared to participants with longer disease duration. Participants reporting BT-related seizures recorded higher scores on one subscale each of MQoL (existential well-being, p=0.02) and BRIEF-COPE (religion, p=0.04). Table 3 provides the summary of results of the tests showing the significant scores (p<0.05).

Table 3: Comparison of disease characteristics, symptoms/impairments associated with the outcome measures (n=36)

Outcome measures	Disease Characteristics & Symptoms/Impairments									
	Gender	Age group**	Tumour type***	Disease duration#	Fatigue	Pain	Cognitive impairment	Visual impairment	Seizures	Speech impairment
MQoL										
Total	0.73	0.28	0.55	0.62	0.92	0.55	0.36	0.71	0.31	0.87
SIS	0.21	0.45	0.07	0.84	0.42	0.69	0.78	1.00	0.54	0.98
Physical symptoms	0.34	0.37	0.93	0.18	0.64	0.81	0.97	0.35	0.34	0.80
Physical well-being	0.48	**0.04**	0.63	0.23	0.69	0.94	0.45	0.58	0.44	0.20
Psychological symptoms	0.88	0.53	0.31	0.69	0.81	0.51	0.21	0.84	0.50	0.58
Existential wellbeing	0.26	**0.01**	0.56	0.78	0.96	0.16	0.40	0.59	**0.02**	0.71
Support	0.54	**0.04**	0.56	0.37	0.60	0.42	0.58	0.86	0.43	1.00
BRIEF-Cope										
Problem focus strategies										
Active coping	0.80	**0.02**	0.38	0.74	0.43	0.23	0.67	0.39	0.10	0.78
Planning	0.37	0.56	0.77	0.38	0.71	0.46	0.49	0.79	0.84	0.82
Acceptance	0.24	0.61	0.58	0.61	0.17	0.33	0.26	0.81	0.71	0.73
Humour	0.67	0.44	0.93	0.78	0.85	0.74	0.41	0.07	0.56	0.85
Religion	0.52	**0.05**	0.95	0.95	0.76	0.73	0.23	0.88	**0.04**	0.78
Using emotional support	0.16	0.83	0.08	**0.01**	0.27	0.27	0.34	0.18	0.14	0.12
Using instrumental support	0.40	0.41	0.25	0.13	0.19	0.41	0.50	0.83	0.07	0.75
Emotion focused strategies										
Self-distraction	0.85	0.53	0.72	0.66	0.34	0.42	0.16	0.38	0.86	0.46
Denial	0.45	0.08	0.45	**0.03**	0.21	0.84	0.77	0.08	0.32	0.89
Venting	0.07	0.80	0.77	0.60	0.72	0.68	0.87	0.48	0.44	0.56
Substance use	0.32	0.35	0.81	0.35	0.73	0.30	0.22	0.49	0.60	**0.04**
Behavioural disengagement	0.22	0.50	0.44	0.17	0.85	0.71	0.31	0.06	0.16	0.63
Self-blame	0.55	0.40	0.74	0.54	0.62	0.57	0.31	0.31	0.93	0.90

*Values significant at 0.05 level (shown in bold)
**Age groups: ≤49, ≥50; ***Tumour types: 1) meningioma, 2) GBM, 3) metastatic; #Disease duration: ≤3 years, 3+ years
MQoL = McGill Quality of Life questionnaire; SIS = Single Item Scale; BRIEF-Cope = BRIEF-Cope inventory

Themes surrounding ACP discussions
Theme A: ACP remains poorly known, understood & documented
Thematic analyses identified low rates of awareness, understanding and documentation in relation to ACP (Table 4: A1-2). Nine participants stated that they have heard of ACP, however only six participants demonstrated understanding of what ACP involved. Five participants were recipients of palliative care services, of which only one participant received ACP information through the palliative care team.

Four participants stated they had received a cancer information pack, however all participants do not recall reading an ACP information brochure (Table 4: A3). There was also lack of ACP documentation amongst BT participants in this study. Out of 38 participants, 13 had a nominated MEPOA, however, only one had a recorded AD and none had a Refusal of Treatment Certificate.

Theme B: Biopsychosocial informants of ACP
The study participants expressed contrasting views on the appropriate timing of ACP discussions (Table 4: B1): some preferred after diagnosis, some after 'coming to terms with the diagnosis', some when they were stable after surgery and initial radiotherapy, many preferred 'anytime' or towards the EOL, but overall, most preferred ACP conversations being conducted prior to EOL stages of the disease course. Several factors impacted on the timing of discussions along the illness trajectory including uncertainty about disease course and prognosis, treatment options and outcomes, cognitive status and religious factors.

Very few participants had ACP discussions with their healthcare providers (Table 4: B2). There was more of a focus on current and near future treatment options depending on progression amongst participants and clinicians, rather than ACP. Some considered families' and/or friends' welfare when considering ACP, with fear expressed amongst BT participants of emotionally burdening their family with these discussions. Others wanted life prolonging treatments to remain alive with young family.

Other perceived challenges to ACP conversations also included young age, personality differences, level of physical and functional status, disease course and prognostic uncertainty, discomfort with the topic, maintaining hope, and feelings of denial, as well as the fear of the irrevocability of AD. Additionally, cultural, religious and spiritual factors, clinician time pressures, rapid specialist clinic appointment sessions and reduced holistic approach were factors that delayed initiation of ACP conversations. Some participants perceived their health care teams as having a narrow focus of care, with limited time given in discussing existential concerns, discussing future care needs or providing comprehensive holistic care. Nevertheless, six participants have had informal ACP discussions to a variable extent with their family and 31 participants in this study did state that that they would be able to have a facilitated ACP conversation if initiated.

Theme C: QoL versus quantity of life
Thematic analyses also identified that most participants placed a premium on QoL as opposed to quantity, consistent with the results of the previous pilot study. QoL was defined in variable ways amongst BT participants (Table 4: C1) and frequently framed in terms of whether an individual would be a 'vegetable', or to be able to think or interact. Participants also placed a high value on mental function and cognition and the possibility of losing those faculties would be a reason to decline further treatment. In most instances, participants made it clear that these factors would be inconsistent with good QoL and would refuse life-prolonging treatment.

Suggested improvement strategies for ACP uptake amongst participants in this study included: provision of knowledge regarding clear and specific prognostic information, individually determined timing of ACP information provision, provision of verbal and written ACP information, education regarding ACP documentation processes, and ability to have facilitated discussions with dedicated health care professionals with holistic care approach and empathy. Time provision for ACP discussions including multiple, split sessions and ACP information delivery to be normalized as routine care for patients were also highlighted by participants.

Table 4: Textual examples informing categories illustrating participants' ACP perspectives

Categories	Text illustrations
A1. Low awareness	"Never heard of it…" "Don't know what that is..."
A2. Lack of understanding	"It is about what to do when you can't make your own rational decisions about finances…" "That they look after you, I don't know more details…" "Yes, I have heard of it; but I don't exactly know the details. As everything was quick, we got a Medical Enduring Power of Attorney. It is about what you want… can't think of examples…"
A3. Lack of information	"I have got brochures from the cancer council and some sent from the hospital but I have put them away and not touched it since…" "I am linked in with palliative care, but I don't have information regarding Advance Care Planning… I only had physiotherapy and music therapy organized…"
B1. Variable views on timing of ACP discussions	"I would probably prefer before you came end-stage, because you are now more yourself and not feeling very sick…" "It depends on whether there is treatment available to prolong my life, I mean we all die eventually… I mean you can have it at any time, I have talked to my family more regarding financial aspects …" "If I felt that treatment wasn't going to give me any benefit, then I'll be happy to talk about Advance Care Planning…" "Never… I have been told that this radiation therapy may not work, and if that happens, I would be extremely disappointed…" "For me, it can be discussed at any time, but preferably when I'm still well and good to talk about it and to be able to make a decision whilst I'm cognitively intact…" "It would be if there is uncertainty about the final outcome about what was happening to me or certainty that the end is near, then I would be happy to talk about it…" "I would prefer it towards the end of life, as my faith does not believe in death…"
B2. Lack of ACP discussions with healthcare professionals	"No… you don't have time when you are in and out, they are so busy… I have not talked to my GP either and I don't have a lot of time with her as well…" "I've spoken to the psychiatrist… but mainly theoretical scenarios; I haven't spoken to my GP about what might happen, but more what is happening at the moment…" "I have been so mobile and capable, we haven't talked about that kind of thing…"
B3. Perceived challenges in ACP discussions (patient & clinician- related)	**Patient-related** "I don't feel so ready that I'm up for Advance Care Planning when I'm hoping to improve" "I don't really want to talk about something as it may not happen…" "Only that it might be locked in just because I feel this way now…" "I think I'm too young to think about it…" "I don't really like talking about it; it's a little bit upsetting…" "Religious factors… and it's also hard when you have children and this is a personal barrier to the conversation we are having…" "It is not easy for me to talk about, and I need more information on my treatment options and disease course…" **Clinician-related** "Doctors and surgeons are too busy…" "I think time is a major barrier, with rapid clinic appointments…." "I think that the more subspecialized medical care is, the less holistic the care becomes…"
C1. QoL versus quantity of life	"I wouldn't want to be resuscitated, I feared seeing someone in advanced stages who couldn't speak… I want to be able to speak and sit up, being able to understand and respond…" "You have got to have some quality of life, you can't just lie in bed… Quality of life for me is to be able to get out of bed at least…" "You want to live a fairly good life.. if you are on a machine, it's not a good life. You want to be able to get around." "Being able to walk, talk, look after myself and for my memory to be preserved are important to me. It would be embarrassing if I didn't recognize someone and they would recognize me…" "I wouldn't want to be in constant pain. I want to be able to get around, to be able to interact with people. If there comes a stage when I can't interact, that's not quality of life. If I'm in a wheelchair, that's fine but as long as I can have a social life." "Not being able to recognize my kids or not being me physically and cognitively is not quality of life for me. If I'm in a wheelchair, that's fine… a small price to pay."

Discussion

This prospective study explored insights from BT patients regarding their experience with ACP, perspectives on the timing of conducting discussions and identified factors that influence future health care decisions and EOL issues. The findings from this study further builds on a previous pilot feasibility study [19]. Firstly, this study highlighted the ongoing limited awareness and discussions in relation to ACP with BT patients who often experience complex neuro-palliative needs. These findings are consistent with existing published literature of ACP in BT patients reporting low rates of EOL discussions and AD completion [20,29]. This issue raises significant gaps in information provision and service delivery with clinical implications, particularly in the context of key national initiatives to promote good EOL care in those with terminal illness, chronic progressive disease, multiple co-morbidities, and in those at risk of cognitive impairment [30].

The findings also identified several factors that influenced BT patients' preferences on timing of ACP conversations, with variable views on when the process preferably occurs. Most felt that conversations should be initiated whilst they are cognitively intact and stable, while others felt that it should ideally be delayed nearer to EOL. Although limited, studies have found variability in the timing of EOL discussions [28]. Delayed conversations are often due to illness and prognostic uncertainty, with patients' preferences in focusing on current treatment outcomes. Some fear that honesty about prognosis will destroy their hope, however, studies have found a variety of responses to wanting support for hope and conversely wanting honest prognostic information. Most patients who do accept the offer of an ACP discussion find such conversations empowering and clinicians should recognize the capacity to integrate hope with trustful communication [27]. Cultural, spiritual and religious factors also play a role in initiation of ACP conversations and patient care preferences. This is consistent with findings of this study which interestingly also found that younger age was associated with higher active coping skills, and using religion to cope with BT course.

Although there is still lack of studies demonstrating the appropriate timing of EOL discussions in BT patients, timely discussions are recommended before individuals become acutely unwell and reviewed over multiple occasions as decisions can change along the disease course [28-30]. This is especially relevant in BT patients due to the uncertainty and progressive nature of the disease course, with progressive cognitive decline and affected decision making capacity skills [30]. These factors may influence their ability to participate in ACP during later stages of the disease process and often results in lack of AD completion. This can often contribute to challenging scenarios for families, who are then frequently left to make EOL decisions. Common EOL decisions in BT patients tend to involve hydration, nutrition, steroid interruption and palliative sedation [9,12,31].

Other barriers for ACP process included: rapid clinic appointment sessions with time pressures, and lack of dedicated health professionals to facilitate conversations. Research has shown that patients do expect health professionals to initiate discussions and want information related to their medical condition, prognosis and to participate in discussions regarding their future medical treatment preferences [32,33]. Another barrier includes the fragmentation of care between primary and secondary health providers, with increasing specialization and complexity of BT treatments, which leads to conversations being increasingly initiated by specialists who provide most follow-up and surveillance of BT patients. Clear communication and collaboration with primary healthcare service providers regarding patients' treatment and care plans will enhance the frequency and quality of ACP conversations with patients. The use of trained non-medical ACP mediators including nursing and allied health, working in conjunction with medical specialists who have been found to be the preferred facilitator, will also be able to offer more available sessions in providing ACP information, and establishing clear and realistic expectations of goals of care verbally [19]. This is in line with other organization initiatives in Australia such as Respecting Patient Choices program [6,34]. Other available methods of establishing robust systems for delivering EOL care include providing patient education sessions, increasing community awareness, staff education workshops and training to increase workforce capacity, and ensuring established system related alerts, documentation, policies, quality improvement processes and governance structures.

Multiple unmet needs amongst cancer caregivers still exist with regards to informational needs relating to prognosis, options for future treatment, practical supportive care strategies, EOL symptom management and ACP delivery [35]. This study found moderate levels of carer burden amongst BT patients, which is consistent with previous qualitative studies that found that the overall caregiver QoL is low [4,5]. Carer stress often results in role reversal within families, physical and financial strain, mood disorders and reduced QoL satisfaction [4]. It is important to note that carers play an important role in the delivery of practical, emotional and EOL support for patients. Studies examining ACP in BT patients and patients' dying with dignity have found that relatives were more satisfied with physician(s) who explicitly discussed EOL decisions with patients [36].

Advances in medical care are resulting in prolonged survival, living and aging with disabilities, including those patients with cancer. Additionally, this study identified that BT patients have a diverse range of symptoms and unique neurological disabilities that impact on their QoL. The needs of BT patients clearly differ from other cohorts of patients with chronic and terminal illnesses. Management of these complex patients should ideally be performed by practitioners with expertise in supportive care of terminal neurological conditions. The delivery of ACP to these patients in the context of a comprehensive neuropalliative-rehabilitation model of care serves not only to improve QoL of patients and families, but also to address symptom burden, physical, functional, psychosocial and spiritual needs [10,37,38]. This model of care highlights the coordination and integration between specialist teams such as neurosurgery, neuro-oncology, rehabilitation and palliative care whose roles often overlap [10]. All teams play a supportive role in being able to deliver ACP information and ultimately, contribute to improving QoL for patients and families. This importance was demonstrated by over half of the participants in this study. The role of health service executives and governance structures is integral in establishing clear expectations, processes and practices for ACP in health care services and organizations, as delivery of ACP works best when seen as a team responsibility. Studies have shown a higher satisfaction rate with overall care in the hospital, as patients are involved in active self-management of their care during their disease course [6]. Health services also need

to work in partnership with culturally and linguistically diverse services to develop appropriate culturally sensitive information that can be delivered to patients, and ensuring access to qualified and trained health care interpreters for ACP conversations.

There were several limitations in this study. The generalizability of findings is limited given the small sample size and participants were recruited from a single, tertiary hospital in a metropolitan setting. Study participants were also at different stages across the illness trajectory. Additionally, the interview population was restricted to those speaking English due to limited funding for translators. Nevertheless, there was a good representation of various cultural groups in this study. Furthermore, as the interview guideline was designed by the researchers, it may have been possible that particular avenues were not explored. An inherent aspect of qualitative methodology is the role of the researcher and the impact of this on all levels of the study method and results. Despite this, there was a commonality to the views expressed by patients and a variety of perspectives were sought. We were also not able to capture the experiences of patients from those treated solely in the private system of care or the views of those who were deemed too impaired to participate. Importantly, however, patients near the EOL were able to offer their insights, providing a unique understanding to their illness experience.

In conclusion, understanding the impact of BT in longer term patients' decision making is important. Timely ACP discussions allows patients to engage in an effective shared decision-making process with their clinicians, thus increasing patient and family satisfaction with EOL care. This study is the first to our knowledge, to examine ACP process in BT patients (majority with high grade gliomas) using both qualitative and qualitative methodology. This study highlights ongoing low rates of ACP discussions and AD completion rates in this population, with difficulty identifying the most appropriate timing of discussions. This gap in practice encourages further higher quality studies in examining ACP in the BT population and to determine the most effective types of ACP interventions to address this gap. ACP is an important tool for inclusion of patients' values, beliefs and preferences to guide future decision-making. It is envisaged that the findings of this study will assist in the service planning and delivery to ensure that needed and appropriate services and supports are coordinated and directed appropriately in this population.

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