The Australian Journal of Cancer Nursing

The Official Journal of the Cancer Nurses Society of Australia

Volume 18 Number 2
November 2017

In this issue

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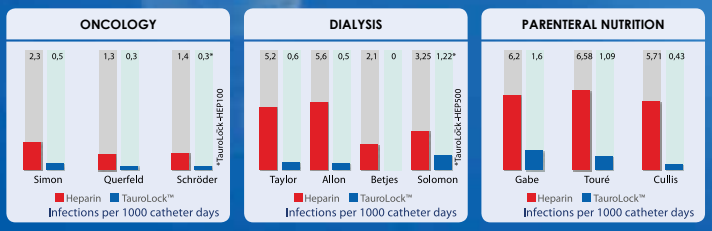

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Ph: 1300 880 441 | Fax: 1300 880 451
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* Punt, C.D., Boer, W.E. Cardiac arrest following injection of concentrated trisodium citrate, Clinical Nephrology, 2008, 69: 117-118. ** Willicombe, M.K., Vernon, K., Davenport, A. Embolic Complications From Central Venous Hemodialysis Catheters; Used With Hypertonic Citrate Locking Solutions, American Journal of Kidney Diseases, 2010, 55: pp 348 - 351. *** Polaschegg, H.-D., Sodemann, K. Risks related to catheter locking solutions containing concentrated citrate, Nephrol. Dial. Transplant. 2003, 18: 2688-2690. **** Schilcher, G. Polaschegg H.D. et al. Hypertonic Trisodium Citrate Induces Protein Precipitation in Hemodialysis Catheters, Selected ASN Meeting Abstracts, 2011

Editorial

The *AJCN* aims to provide a forum where debate and the exchange of views can take place. We welcome papers on contemporary professional policy or practice issues of concern and interest to cancer nurses.

Notes for contributors

All correspondence relating to the journal should be directed to the editors. Guidelines for contributors to the journal can also be obtained from the editors. The *AJCN* is published twice a year.

ISSN 1441-2551

The Australian Journal of Cancer Nursing

Volume 18 Number 2 — November 2017

Publisher

CAMBRIDGE PUBLISHING

A division of Cambridge Media
10 Walters Drive, Osborne Park, WA 6017
Tel: (08) 6314 5222 Fax: (08) 6314 5299 Web: www.cambridgemedia.com.au

Copy Editor Rachel Hoare Graphic Designer Gordon McDade

Editorial

Nursing challenges in caring for adolescents and young adults with cancer

Challenges in cancer nursing are experienced across the world. Some challenges are nuanced and specific to individual countries and some touch all of us wherever we work. In this guest editorial, Professor Mitsue Maru, who was recently in Australia visiting the University of Wollongong and who is from the Konan Women's University in Japan, explores some of the challenges that affect us all.

Mitsue Maru • RN, DSN
Professor International Nursing Development, School of Nursing & Rehabilitation, Konan Women's University, Higashinada-ku, Kobe, Japan

Recent studies in major Western countries have shown that there are significant gaps in survival rates between adolescents and young adults with cancer (AYA) and other age groups with cancer. Little is known of the survival rate of this population in Japan. Under the leadership of Dr Keizo Horibe, a paediatric oncologist, multidisciplinary study groups started to explore issues of AYA in 2015.

Although the analysis of the responses of nearly 2000 nurses has not yet been completed, we, the nursing team of Dr Horibe's project, have discovered some interesting findings and may conclude that Japanese nurses are not yet fully aware of AYA's specific issues, such as fertility; social and romantic relationships; education and career trajectories and how they are being affected by cancer diagnosis, treatment, and survivorship challenges. The data also suggest that nurses who experienced the death of AYAs undergo more severe psychological damage than those who experienced the death of aged patients. Specific knowledge and skills on AYAs will be needed in addition to new models of care delivery, although there are many obstacles for multidisciplinary teams, including nurses. The following describes some of the challenges in Japan, which have commonalities with Australian experiences.

Japan is an ultra-ageing society, with 26.7% of the population being over 65 years old. Cancer has been the leading cause of death since 1981, and it currently accounts for almost 30% of deaths in Japan. The National Health Insurance system and Social Welfare systems are well developed to support these ageing populations. There are significant concerns, however, that these systems are not adequate to support younger cancer patients.

Japan has two kinds of qualified nurse — licensed practical nurse (LPN) and registered nurse (RN) — in a total of 1.6 million employed nurses. To be an RN, students must complete basic nursing education in either diploma school, college (associate degree), or a four-year university program (bachelor degree) and then sit for national licensure examination provided by the Ministry of Health and Welfare. In 2017, Japan has 255 BNS programs, 165 MSN programs, and 88 PhD programs in universities, which is the largest among Asian countries.

Certified nurse specialists (CNS) are categorised into 13 different specialist fields including cancer nursing. They are educated at master level and need to take a certification examination held by the Japanese Nurses Association. CNSs with cancer nursing specialisation comprise the largest group among CNSs, but it accounts for <1% of all nurses populations.

There are 400 designated cancer hospitals and 34 cancer community hospital in Japan; however, there are few hospitals with AYA units. Because of diverse diagnosis in this population, especially during late teenage years to the early twenties, there are few specialist nurses, neither in child-oriented hospitals nor adult ones.

We are facing never-known new challenges in the history of cancer nursing. Sharing our experiences and knowledge with nurses abroad and developing nurses' networks with enthusiasm for quality of care for AYAs with cancer will help patients, families, friends, loved ones, and nurses themselves. In this, cancer nurses in Japan and in Australia share a common need.

Supportive care screening in rural ambulatory cancer care

***Cynthia A Opie** • RN, BA Nursing, BA PH, MPH/TM (in prog)
Research Fellow, University of Melbourne, Department of Rural Health and Echuca Regional Health, Echuca, VIC 3564, Australia
Email: copie@erh.org.au

Alison Koschel • RN, DipApp, GradDip HP, PhD
Research Consultant, University of Melbourne, Department of Rural Health, Shepparton, VIC 3632, Australia

Kaye E Ervin • RN, BA Ed, MEd, PhD (c)
Research Fellow, University of Melbourne, Department of Rural Health, Shepparton, VIC 3632, Australia

Lynette Jeffreson • RN, GradDip Nursing
Medical Day Treatment Unit Manager, Echuca Regional Health, Echuca, VIC 3564, Australia

Helen M Haines • RN, GradDip Midwifery, MPH, PhD
Senior Research Fellow, University of Melbourne, Department of Rural Health, Shepparton, VIC 3632, Australia

*Corresponding author

Abstract

Aim

To explore supportive care screening evaluating cancer-related distress and subsequent referrals to supportive care services.

Method

Mixed method observational study including data from a retrospective medical file audit and a cross-sectional, self-report questionnaire was conducted with rural ambulatory cancer patients.

Results

Audit data showed a high distress rate of 40% (n=242). Twenty-nine per cent (n=28) of people in high distress (n=96), received a referral. Attendance to referrals was 53%. Questionnaire data found 32 (32%) reporting high distress (n=104). Men reported lower quality of life; there was less satisfaction with the information provided and lower participation in referrals than women.

Conclusion

High distress prevalence was consistent with that previously reported in populations of cancer survivors. Referrals for supportive services were low and attendance was poor. Men reported overall poorer outcomes than women, possibly indicating gender variance in supportive care needs in this rural setting.

Introduction

Distress in patients with cancer is common with at least a third of this population group experiencing high distress[1,2]. Physical, social and emotional problems may individually or collectively cause distress and present anywhere along the cancer care continuum, from initial diagnosis to after completion of treatment[3]. Unrelieved distress has negative impacts on a person's capacity for effective decision making, adherence to medical recommendations, and treatment outcomes[4-7]. More than two-thirds of people with cancer in Australia achieve five-year survival[8]. The importance, therefore, of recognising and alleviating distress is paramount to their quality of life.

Rural disparities in health outcomes are well known in Australia[9,10] and cancer is no exception[11]. Rates of cancer survival are higher for people in urban environments or cities compared to rural populations[11,12]. In an attempt to achieve equitable outcomes for all Victorians and improve rural disparity, Victoria's Cancer Action Plan 2008–2011[13] was implemented almost a decade ago. The plan placed an emphasis on improving the infrastructure in regional communities and linking healthcare across the state (p. 47)[13]. To facilitate this process, Integrated Cancer Service networks were tasked with supporting the implementation of routine assessments and screening[13,14]. Supportive care screening was one such assessment introduced to identify cancer-related distress[14] and became routine practice in the rural region of this study in 2011[15].

Screening for cancer-related distress is conducted through the use of a supportive care screening tool, which contains an 11-point distress thermometer and accompanying problem checklist that assesses practical, family, emotional, spiritual/religious and physical life domains[14]. A self-reported distress

thermometer score of four or more is considered consistent with moderate to severe distress (herein referred to as high distress) and warrants further evaluation and appropriate intervention[1,16,17]. The goal is to mitigate distress and maximise quality of life through referral to appropriate supportive services[18].

To date there is no evidence that explores the prevalence and management of cancer-related distress in rural communities. This research, therefore, aimed to identify the prevalence of high distress and to explore the frequency, type and uptake of referrals in one rural Victorian health service where supportive care screening has been practised since 2011.

Method

Design

This study was undertaken in 2015 using a mixed method observational design with retrospective file audit data of medical records and a cross-sectional, self-report questionnaire of cancer patients.

Setting

The setting was a rural ambulatory cancer care service in northern Victoria, Australia, where supportive care screening is routinely conducted by specialised cancer support nurses with cancer patients.

Participants

Potential participants were identified using the ambulatory care oncology unit register where patient demographic details and service activity was recorded during the period from November 2011 to 18 November 2015. The supportive care screening tool contained in the medical files of patients aged between 18 and 100 years was audited. Patients were subsequently invited by letter to complete a self-report questionnaire and those who agreed to do so signed a written consent form and returned the questionnaire by reply-paid post. Patients identified from the medical record audit as deceased or in end-of-life care during the study period were excluded from receiving a questionnaire invitation.

Measures

1. An audit template was developed for the study and was used to record the following outcome measures from the supportive care screening tool in the medical record:
    - *Distress as recorded on the distress thermometer.*
    - *Reasons for distress as recorded on the problem checklist (five domains: practical; family; emotional; spiritual/religious; physical).*
    - *Tumour stream, current treatment regime and screening point in cancer experience.*
    - *Referrals: frequency, destination and acceptance.*
2. A self-report questionnaire was developed incorporating:
    - *Questionnaire data included: demographics, cancer type and time since diagnosis and treatment received.*
    - *Number of occasions of ambulatory cancer care use (including treatments, specialist nurse appointments, phone calls, admissions and home visits).*
    - *Using 0–10 visual analogue scale participants were asked to rate their experience of how they were treated by the cancer support nurses, with zero equal to "poor" and 10 equal to "excellent".*
    - *On a three-point Likert scale participants were asked to indicate how helpful the information provided by the cancer support nurses was, from "not at all helpful" to "completely helpful".*
    - *Participants were asked to rate their "overall health" and "quality of life" on two seven-point visual analogue scales, with one equal to "very poor" and seven equal to "excellent".*
    - *Participants were asked to rank their current level of "worry" on a visual analogue scale where zero is equal to "not at all worried" and 10 equals "extremely worried".*
    - *Referrals were explored via participants selecting service use from a list of supportive care service types (health professionals, support groups, websites and peak bodies), whether contact was made by that service, if placed on a waiting list, attendance and further use of that service.*
    - *Three short-answer questions relating to support and cancer experiences were included.*

A copy of the survey is available from the corresponding author.

Data analysis

All file audit data was entered by two members of the research team into a password-protected Microsoft ACCESS © database and then transferred to STATA© software (Version 8). The continuous measure of distress was recoded into a binary variable at the cut point of ≥4 on the distress thermometer, which was coded as high distress. Descriptive univariate and multivariate statistics were used to determine the outcome measures in all quantitative data. Proportions were compared using Pearson chi-square and continuous measures were compared using independent t-tests. Free-text responses were explored using a content analysis approach.

Ethics approval

Ethics approval to conduct the study was granted by the regional Human Research Ethics Committee (approval number HREC/44/15).

Results

Medical file audit

Characteristics

In total, 242 medical records were audited (140 from the cancer support nurse and 122 from a specialist breast care nurse). Participants were on average 66 years of age and almost three-quarters were women. The largest cancer stream was breast followed by colorectal. Table 1 describes the characteristics of the audited population.

Table 1: Demographics and descriptive profile of patients in file audit

	N=242	%
Age in years mean 66 (SD 13)		
Gender		
Female	175	72.6
Male	66	27.4
Diagnosis		
Breast cancer	124	51.0
Colorectal cancer	32	13.2
Genitourinary cancer	17	7.0
Lung cancer	15	6.2
Gynaecological cancer	12	4.9
Haematological malignancy	12	4.9
Other: GBM, cholangio, pancreas, metastatic, upper GI, skin, head and neck cancers	27	10.3
Treatment regime		
Surgery	20	8.2
Pre-surgery	19	7.8
Post-surgery	37	15.2
Chemotherapy	62	25.5
Radiotherapy	25	10.3
Palliative care	1	0.4
No treatment	55	22.6
Screening point		
Diagnosis	37	15.2
Commencement of treatment	28	11.5
During treatment	59	24.3
At conclusion of treatment	21	8.6
During follow-up	56	23.0
Screens completed		
Screened once	124	51
Screened more than once	118	45

Distress

At initial screening the mean distress score was 3.1 (SD, 2.7). Ninety-eight patients (40.5%) were classified high distress. There was no difference in the prevalence of high distress between men and women (p=0.50). High distress was significantly higher than low distress at two points throughout cancer care: diagnosis (59.5%, n= 22) and end of treatment (61.9%, n=13) (p=0.009).

Reasons for high distress

Statistically significant variations in problems contributing to distress are shown in Table 2. Those in high distress were more likely to report issues across many aspects of all domains, with the exclusion of fatigue and sleep problems and transport, which were more frequently reported by people in low distress. Those with low distress also reported less worry and less nausea than the highly distressed.

Referrals

Forty-nine per cent (n=47) of patients in high distress received a referral for some form of supportive care compared with 25% (n=36) of people in low distress (p <0.001). Of the high distress group 51% (n=39) did not receive any referrals. People experiencing high distress were more likely than those in low distress to be referred to social services (p=0.02) and palliative care (p< 0.01). Irrespective of the level of distress, 23% (n=56) of people overall refused a referral when offered.

Questionnaire

Response

All screened patients who were living, not in end-stage palliation and had a known current address were mailed the questionnaire to complete. A total of 195 questionnaires were sent. The first mail-out achieved a response of 46% (n=89 people), a reminder second mail-out was conducted two weeks after the first, which resulted in a further 15 questionnaires (10%). A total of 104 questionnaires (53% response rate) were analysed.

Characteristics

Table 3 shows that demographics of the survey respondents were reflective of the medical file audit. Seventy-five per cent were women. Men who responded were more likely to be older than the women (72.0 years compared with 65.5 years, p=0.02). Greater than half had their cancer for over two years and the majority of people receiving supportive care at the study site had received their cancer treatment at another hospital. Almost all respondents (96%) had undergone supportive care screening six or more times.

Distress

Reported level of distress was negatively skewed with Median 1 (IQR 0, 5). High distress was reported by 32 (32%) of respondents. There was no difference in the proportion of high distress reported by women compared to men.

Overall health, quality of life and level of worry

Overall health and quality of life in the past week was measured on seven-point visual analogue scale — the mean score for overall health was 5.3 (SD 1.1) and the mean score for quality

of life was 5.5 (SD 1.2). Level of worry about life circumstances was measured on a 10-point visual analogue scale and the mean score was 3.2 (SD 3.0).

Overall health, quality of life and worry were then dichotomised with cut point of ≥ 6 = high and ≤ 5 = low. Those in high distress were more likely to: rate their overall health as low (n=26, 81.2%) p<0.001; rate their quality of life as low (n=24, 75%) p<0.001 and their worry as high (n=18, 58.1%) p<0.001. Men were (n=15, 60%) more likely than women to report low quality of life (n=28, 36.4%) (p=0.04).

Referrals

Eighty-two people (85.4%) reported having received a referral. More people in the low distress group (n =51, 64%) reported having received a referral than the high distress group (n=29, 36%).

Those living close to the health service (within 24 km) were more likely to accept a referral (n=65, 90.3%) than those living greater than 25 km (n=17, 70.8%) (p= 0.02) and women (n=65, 87.8%) accepted referrals more than men (n=13, 59%) (p =0.002).

Responders were asked to indicate whether they were placed onto a waiting list for the referred service, if they actually attended the appointment and, if so, their perceived usefulness of the service.

Low numbers (n=10, 12.2%) of responders reported being placed on a waiting list. Of those who did attend their appointment, very few (n=11, 13.4%) found the service to be useful. Non-attendance at referral appointments occurred on average 40% of the time across all services.

Reasons for non-attendance at appointments

Participants were asked to use free text to describe reasons for non-attendance to an appointment. Twenty-nine people (28%) provided a response. More than half reported not attending an appointment due to being "not interested" (n=16, 55%). Almost a quarter of non-attendance was attributable to being "too unwell from treatment" (n=7, 24%). Other reasons for non-attendance included work commitments, preference for an alternative service provider or distance from the service.

Information provision

Sixty-three people (97%) found the information they were provided by the supportive care team to be completely helpful; however, men were less likely to find the information completely helpful compared to women (p=0.004).

Table 2: Statistically significant results of the problem checklist for reported high and low distress

			High distress	Low distress	
Problem/Issue	**n**	**%**	**n (%)**	**n (%)**	**P value**
Practical problems					
Insurance	44	18.1	24 (54.6%)	20 (45.4%)	0.001
Work	18	18	12 (66.7%)	6 (33.3%)	0.001
Transportation	34	14.1	16 (47%)	18 (52.9%)	0.04
Housing	12	4.9	9 (75%)	3 (25%)	0.001
Family problems					
Partner	26	10.7	16 (61.5%)	10 (38.5%)	0.001
Children	17	7.4	10 (58.8%)	7 (41.2%)	0.01
Emotional problems					
Nervousness	75	30.9			
Fears	71	29.2	44 (61.9%)	27 (38.1%)	0.001
Sadness	68	27.9	39 (57.3%)	29 (42.6%)	0.001
Loss of interest in usual activities	45	18.5	28 (62.2%)	17 (37.8%)	0.001
Depression	39	16.1	28 (71.8%)	11 (28.2%)	0.001
No worry	130	53.7	21 (16%)	109 (83.8%)	0.001
Physical problems					
Fatigue	143	58.8	58 (40.8%)	84 (59.1%)	0.001
Sleep	103	42.4	42 (40.8%)	61 (59.2%)	0.01
Memory/concentration	86	35.4	38 (44.2%)	48 (55.8%)	0.002
Pain	65	26.9	36 (55.4%)	29 (44.6%)	0.001
Appearance	38	15.6	25 (65.8%)	13 (34.2%)	0.001
Not being nauseous	215	88.8	64 (29.8%)	151 (70.2%)	0.05
Not being constipated	203	83.8	59 (29.0%)	144 (70.9%)	0.004

Cancer experience

Respondents were asked to respond in free text if there was anything that resulted from supportive care screening that made a positive difference to their experience of cancer: 32 people (30.77%) commented. A majority of responses emphasised improvements in emotional and psychological support for themselves and their family members, a better knowledge of available services, local access to services resulting in less travel and improvements to their quality of life.

Discussion

Five years of supportive care screening in a regional health service was explored to determine the prevalence of high distress, and the frequency, type and uptake of accompanying referrals. Initial supportive care screening identified a high distress prevalence of 40%, with peaks at diagnosis and the end of treatment. Highly distressed patients were more likely to be provided with a referral at the time of supportive care screening; however, overall attendance at referrals was low, regardless of distress. High distress was reported by more than one-third of respondents in the self-report questionnaire, with the low distress group reporting a higher number of referrals for services. Men and women reported similar rates of distress; however, men were more likely to experience a reduced quality of life. Similarly, overall satisfaction with the ambulatory cancer care team was high, but men were less likely than women to find the information provided as useful.

High distress prevalence is reported in the literature to vary significantly (33.2% to 89.1%), with greater distress associated with disease stage, younger age, female gender and high rates of pain[2,19-21]. Akin to our research, Wang and colleagues[21] did not find that cancer type was associated with higher rates of distress. However, we found that high distress was associated with two key time points: diagnosis and end of treatment. These are commonly identified periods for increased vulnerability risk, according to the National Comprehensive Cancer Network[3].

Diagnosis is an existential crisis point as patients come to terms with shock and treatment decisions[5,6]. At the end of treatment some patients may feel a sense of being "untethered" from the highly intensive focus of clinicians and rigorous treatment regimens leaving them feeling "exposed" and at risk. Further to this, high distress was found in one-third of the follow-up group of questionnaire respondents (who on average were two years post-diagnosis) suggesting that distress persists or re-emerges well beyond the initial treatment phase. Advancing disease, new disease[22], prolonged treatment regimens or possibly less regular contact with health care practitioners may explain new or persistent distress. It is important to consider, though, that in this group of rural patients the average age was 66 years. Deimling explains that cancer-related worry is an important consideration in older people (age 60+ years) surviving cancer, particularly as advancing age often fosters new health challenges and subsequent concern about linkages between symptoms and their cancer[22].

Table 3: Demographics of questionnaire group

	N = 104	%
Age in years mean 67.1 (SD 12.1)		
Gender		
Males	26	25
Females	78	75
Lived distance from service		
Less than 25 km radius	80	77
Greater than 26 km radius	24	23
Diagnosis		
Breast	56	55.4
Other (colorectal, head & neck, lung, lymphoma, melanoma, ovarian, prostate, stomach)	26	25.7
Multiple	19	18.8
Time since diagnosis		
Less than 24 months	43	42.5
Greater than 25 months	58	57.4
Treatment received at study site		
Chemotherapy only	10	9.9
Chemotherapy + supportive care	26	25.7
Supportive care only	7	6.9
Treatment at another hospital + study site supportive care	58	57.4

Our findings did not show gender differences in the prevalence of high distress in either the medical file audit or in the self-report questionnaire. This contrasts to reports from a large North American ambulatory cancer care multisite study, which showed high distress was significantly correlated with being female[23]. Of interest, however, was in this rural cohort men were more likely than women to report low quality of life. Previous studies have also shown that men with cancer experience some very specific unmet needs[24]. A large systematic review focussing on the unmet supportive care needs of men living with and beyond prostate cancer describes problems related to intimacy, lack of clear information, and physical and psychological distress[25]. Poor quality of life after cancer treatment is commonly reported by men[26]. In line with previous studies[1] our study found that questionnaire respondents in high distress were more likely to rate their overall health and quality of life as low and their worry as high.

It is unclear if this is related to gender or to their particular tumour stream. The distress thermometer and the problem checklist have been tested widely with both men and women[3]; nevertheless, perhaps in this cohort of rural men "quality of life" carries greater meaning than "distress". Possibly these rural men found it more palatable to reveal issues with quality of life than to describe themselves as distressed.

High distress was associated with almost all domains of the problem checklist. Feelings of depression were recorded in over 70% of the audited files of patients in high distress. Negative emotional states such as *"worry, fears, nervousness, sadness, depression and trouble sleeping"* are frequently reported by people with cancer[27,28]. Financial stress related to household expenses, debt, borrowings and selling or refinancing the family home are known to increase stress and hardship for people with cancer[29] and were more prevalent in the highly distressed group.

Importantly, the file audit showed that regardless of the level of distress, one in five patients declined a supportive care referral and approximately only one-third of people screened were provided a referral. In contrast, nine out of 10 respondents to the questionnaire self-reported having received a referral. It is unlikely that only the respondents who received a referral at screening participated in the questionnaire; therefore, it might be that this mismatch is explained by referrals potentially being generated from multiple sources outside of the regional supportive care screening. Well over half of respondents reported receiving their cancer care, including supportive care screening, at another hospital in addition to the rural ambulatory site. Respondents were not asked about the referral source, so this outcome may only be speculated and further research is warranted to understand this in more detail. Greater transparency in care coordination between service providers minimises duplication of care and offers opportunities to truly identify gaps in service[14].

Intuitively, the medical record audit showed that patients reporting high distress were more likely to receive a referral than those in low distress. Contrary to the intention of the supportive care screening process, however, we found that over half of patients reporting high distress were not referred at all. The National Cancer Control Network recommend that people found to be in high distress during screening ought to be considered for a referral for psychosocial services[3]. Linehan and colleagues, in their South Australian study, similarly found that referrals were low, despite levels of high distress[30]. It was postulated that nurses may use more than the distress thermometer to assess a need to refer[30] and as a clinical nurse specialist in cancer care, may themselves be equipped to mitigate distress at the time of screening. Further research is needed to explore the clinical reasoning and shared decision making that takes place with supportive care screening nurses and the patient, in addition to what services the patient may already be accessing from alternative referrers.

Almost one in five people refused a referral when offered and, of those who did accept a referral, at least four out of 10 did not attend the appointment. Reasons for non-attendance were largely due to disinterest and being unwell; however, a few stated that the distance from the provider was prohibitive. In parallel, it was noted that a person was more likely to accept a referral if they lived within 24 kilometres of the health service. In all countries, travel distance to appointments is a major factor in health care decisions[31]. Disparities in rural health as a result of geographical distance to services are well recognised[32].

The majority of the referrals generated during screening in this study (both identified in the medical record audit and the questionnaire responses) were for social needs and physiotherapy. Phillips reports that surviving cancer is impacted by physical and psychosocial needs and consequently is an important public health issue[33]. Half of those referred to social services reported that they did not attend the appointment and almost a quarter of those who did attend reported limited usefulness. Of all respondents that attended any supportive care appointments, only 20% indicated that the service was useful. Of particular interest was that men were less likely than women to find the information provided at supportive care screening as useful. When coupled with the finding that men reported a lower quality of life than women, this is an area that warrants further enquiry within the rural context.

Limitations

Only half of the patients identified from the audit, and invited to complete the questionnaire, responded. It may be that non-responders were reflective of people with poorer quality of life, ongoing or recurrent illness, or other competing interests such as returning to work.

Respondents in this study were predominantly female, had a diagnosis of breast cancer and were on average over 60 years of

age and as such this limits the ability of the study to represent a broader population of people with a cancer diagnosis, but cancer is a disease of ageing and more prevalent in the breast of women. Additionally the cross-sectional design of the survey means that the findings from that arm of the study relate to the feelings of the respondents at one point in time.

Conclusion

High distress prevalence in this study was consistent with that previously reported in populations of cancer survivors. Referrals for supportive services were low and of those referred, attendance at appointments was poor. Further investigation into clinician decision making and appropriateness of referrals to specialised services for cancer-related distress is needed as is the effectiveness of the overall integration of care from multiple providers. Men reported overall poorer outcomes than women, possibly indicating gender variance in supportive care needs in this rural setting.

Acknowledgements

This research was supported by the Australian Government Department of Health through the Rural Health Multidisciplinary Training Programme and the Loddon Mallee Integrated Cancer Services (LMICS).

Funding

The Loddon Mallee Integrated Cancer Services (LMICS) provided funding for this research.

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The minimum education and safety requirements for the nursing administration of cytotoxic drugs: an integrative review protocol

*** Elisabeth Coyne** • RN, MN Hons, PhD
Senior Lecturer, School of Nursing & Midwifery, Menzies Health Institute Queensland, Griffith University, QLD, Australia
Email: e.coyne@griffith.edu.au

Sarah Northfield • RN, BN, GradCert (Cancer Nursing)
Clinical Nurse (Research), Cancer Care Services, Royal Brisbane and Women's Hospital, Herston, QLD 4029, Australia

Kylie Ash • RN, MN
National Project Manager, School of Nursing, Queensland University of Technology, Kelvin Grove, QLD 4059, Australia

Leisa Brown-West • RN, BN, Cert Chemo Reconstruction, Grad Cert Onc, GDip AdVocEd, MN (Cancer Nursing)
Clinical Implementation Manager, ICON Integrated Cancer Centre, North Lakes, QLD 4509, Australia

Corrie Miles • EN
Ambulatory Oncology, Townsville Cancer Centre, Townsville Hospital, Douglas, QLD 4814, Australia

Karen Munton • RN
Clinical Practice Development Nurse, Day Oncology Unit, Sunshine Hospital, St Albans, VIC 3021, Australia

Catherine Barratt • RN
Staff Development Educator, WA Cancer & Palliative Care Network, System, Policy & Planning Division, Department of Health, East Perth, WA, 6004, Australia

* Corresponding author

Abstract

Background: This protocol describes the steps taken to develop an integrative review to identify current research on the minimum education and safety requirements for nurses to administer cytotoxic drugs. The review will provide evidence to underpin a Cancer Nurses Society of Australia (CNSA) position statement on the same topic.

Methods: An integrative review of literature will be conducted within the following databases: CINAHL, PubMed, the Cochrane Library and Embase. Methodological quality of the included studies will be assessed using the Mixed Methods Appraisal Tool.

Discussion: The completion of an integrative review will ensure CNSA takes a leadership role in the provision of evidence to inform cancer nurses about the minimum education and safety requirements when administering cytotoxic drugs in any setting.

Conclusion: A systematic approach to the development of a CNSA position statement will provide transparency on the supporting evidence. Gaps in the current literature will be identified, highlighting future directions for research.

Keywords: Safety, education, cytotoxic drugs, protocol.

Background

The Cancer Nurses Society of Australia (CNSA) aims to provide resources which support and contribute to cancer nursing practice. The CNSA has previously provided a position statement outlining the minimum education and safety requirements for nurses to administer cytotoxic drugs in any setting. To maintain the currency and rigour of this document, a literature review will be conducted using the current integrative review protocol. It is important for nurses to understand the minimum safety and education requirements when administering cytotoxic drugs and the evidence supporting these recommendations.

To ensure patient safety, nurses must receive appropriate education on cytotoxic drug administration. The Antineoplastic Drug Administration Course (ADAC) offered by EviQ[1] provides standardised education for the safe administration of antineoplastic drugs and handling of related waste via online modules, a skills workshop and competency assessments in the clinical setting. The evidence that informed the development of the ADAC modules, along with a systematic, integrative review will be used to update the CNSA position statement for the minimum education and safety requirements for the nursing administration of cytotoxic drugs.

It is important for the minimum standards to be based on current evidence and for the development of these standards to be replicable[2]. Specialist knowledge, competencies and skills are required by health care professionals to administer cytotoxic drugs[3]. Standards of practice provide guidelines for education and safety, to ensure nurses have the essential knowledge to administer cytotoxic drugs in a way which is safe for both the patient and the nurse[4]. Cytotoxic drugs are intended primarily for the treatment of cancer and have a highly toxic effect on cells[5]. In the context of this integrative review, "cytotoxic drugs" will refer to all chemotherapies except for targeted therapies, such as biotherapy agents or monoclonal antibodies.

Cancer nurses are required to have knowledge about the pathophysiology of cancer and mechanism of actions for cytotoxic drugs[2,6]. The nurse administering the cytotoxic drugs needs to have assessment skills to complete a situational assessment of the patient and the venous access point to ensure safe administration and prompt identification of adverse reactions[4]. The nurse should also be able to assess the patient and family across the domains of health, including physical and psychosocial, to ensure best patient and family outcomes during treatment and into survival[7,8]. A minimum education standard for nurses administering cytotoxic drugs provides clear guidelines to ensure nurses are equipped with the essential knowledge to administer drugs safely for their own safety and that of others.

The safe administration of cytotoxic drugs has been a contentious issue with differing practices across institutions and countries; however, a minimum standard provides a guideline for best evidence-based practice[4,9]. Detailed information about safe administration should include safe handling, accidental exposure and provision of patient and family safety education to ensure they have an understanding of side effects/toxicities and are able to make informed decisions and manage their own health care[10,11]. The complexity of cytotoxic drug administration increases the potential for errors. The variations of medications, administration routes and the co-morbidities of patients adds to the complexity which the cancer nurse must navigate to provide safe cytotoxic drug administration and reduce potential errors and negative outcomes for the patients[12]. The development of evidence-based, high-quality standards of practice work towards providing nurses with guidance to aim for best and safe practice for patients and nurses.

The purpose of developing a protocol ensures methodological decisions, search terms, data extraction and synthesis are considered, justified and replicable. This process improves the quality of the literature review and enables the final product to be based on current available evidence[13]. A well-developed protocol provides a baseline for future literature reviews, which in the case of a position statement will inform revisions and updates of the document to ensure it is based on current evidence[13].

Methods

The current integrative review protocol was developed by the project team who are members of the CNSA Education Committee. All research questions should be specific and well articulated to identify relevant research on the topic of interest[14]. One approach to construct a research question is the PICO format, which employs the following components: (P) the patient, population or problem being addressed; (I) the intervention or area of interest; (C) the comparison intervention (if applicable); (O) the outcomes of interest[14,15]. The project team worked collaboratively to develop search terms using the PIO format (population, interest, outcomes) (refer to Table 1). A review protocol enables consistency in the data extraction, critique and synthesis, reducing the ambiguity of staying focused on the research question. This review framework was developed to guide an integrative review across two key areas — minimum education and safety requirements for nursing administration of cytotoxic drugs. This review will inform the development of the 2018 CNSA position statement on the minimum standards for education and safety requirements for nursing administration of cytotoxic drugs in any clinical setting.

An integrative review design guided by the Whittemore, Knafl[16] framework will be used to explore qualitative, quantitative and mixed method, ensuring a comprehensive review of research. The Whittemore, Knafl[16] framework includes problem identification, literature search, data evaluation, data analysis and synthesis.

Problem identification

The research question was developed in the process of identifying the aims and focus of the new CNSA position statement. Education and safety requirements were combined in the research question after literature identified the connected nature of these key requirements when administering cytotoxic drugs[4]. A range of keywords were identified during the scoping and preliminary literature search phase. These were further refined during completion of the literature review, resulting in the following key terms, which provided a comprehensive review of literature exploring the minimum education and safety requirements for nurses to administer cytotoxic drugs.

Inclusion and exclusion criteria

The inclusion criteria for this integrative review will be peer-reviewed primary research published during 2006–2017 using quantitative, qualitative or mixed methods, which report research findings on *education and safety requirements for nursing administration of cytotoxic drugs in any setting* (refer to Table 2). Grey literature will be reviewed for best practice recommendations for nursing administration of cytotoxic drugs made by cancer-focused Australian and international health care professional societies/associations/organisations to inform the background of this review. Papers that describe nursing administration of targeted therapies, such as biotherapy agents

Table 1: PIO search terms — integrative review

Question component	Key term	Search synonyms	Final search synonyms
Population	Nurses registered with AHPRA	**Nurses** Nurs* "registered nurse" "enrolled nurse" "Oncology nursing" "Cancer care nursing" "Cancer nurs*"	**Nurses** "Nurs*"
Interest	Minimum safety and education requirements for the nursing administration of cytotoxic drugs	**Safety** "safe practice" "cytotoxic safety" "safe handling" "cytotoxic waste" "workplace health and safety" "occupational health and safety" "cytotoxic exposure" "cytotoxic-related waste" "occupational exposure" **Education** "training" "educat*" "competen*" "skill*" "standards of practice" "guidance" "preparation" "recommendations"	**Safety** "safe practice" "safe handling" **Education** "educat*" training "skill*" preparation recommendations
Outcome measures	Nursing administration of cytotoxic drugs	**Administration** "chemotherapy administration" "cytotoxic drug administration" "anti-neoplastic drug administration" "anti-cancer drug administration" **Cytotoxic drugs** Chemotherapy "Anti-cancer drug*" "anti-neoplastic drug*" Cytotox* "cancer medication" "anti-cancer medication" "cancer treatment" Mutagenic Carcinogenic Teratogenic Genotoxic	**Administration** Administration "chemotherapy administration" **Cytotoxic drugs** Chemotherapy "cancer treatment"

and monoclonal antibodies will be excluded. In addition, operational clinical guidelines and papers describing legislative requirements and registration requirements outside Australia will be excluded. Only research articles published in English, where full text-article is available will be included.

Table 2: Inclusion and exclusion criteria

Inclusion criteria	Exclusion criteria
• English language only • Full-text article available • All patient diagnostic and age groups • All health care settings • Provides primary evidence supporting any education or safety requirement for the nursing administration of cytotoxic drugs by all routes • All study designs • Studies published in 2006 – June 2017 • Peer-reviewed primary research or grey literature articles, including quality improvement reports	• Papers that describe nursing administration of targeted therapies, such as biotherapy agents or monoclonal antibodies • Papers that provide operational clinical practice guidelines • Papers describing legislative requirements and registration requirements in settings outside Australia

Literature search

A comprehensive literature search will be conducted across the following databases: CINAHL with full-text EBSCO Nursing and Allied Health; PubMed (which includes Medline and Pre-Medline) Health Sciences; The Cochrane Library and Embase using a combination of key words and MeSH terms (Table 1). For each database, a specific search strategy will be developed. In PubMed, terms will be combined as MeSH and title/abstract, in EMBASE and PsycINFO as subject heading and keyword, in CINAHL as subject heading and title/abstract, in CENTRAL as MeSH and title/abstract/keyword, and in Web of Science as topic.

In addition to these electronic database searches, a grey literature search will be conducted (using Google) to identify relevant practice recommendations, key guidelines, position statements, educational resources, competency and professional standards related to nurse administration of antineoplastic drugs made by international and Australian cancer-focused health care professional societies/associations/organisations. Findings from the grey literature search will be used to inform the background section of the integrative review. After literature searches have been completed, reference lists of ADAC will be hand searched to identify any additional relevant papers. Hand searching the reference lists of relevant articles will also be performed, to ensure all articles that met the inclusion criteria are screened as part of the integrative review process. A spreadsheet will be developed to track the article retrieval process and direct uploading of included articles into an online EndNote Library© to maintain an up-to-date reference list.

Literature searches, screening of search results and articles will be completed across the selected databases and secondary searches completed from reference lists. Decisions on whether to include studies will be made based on the inclusion and exclusion criteria (Table 2). For journal articles where relevance cannot be determined by reviewing the title and abstract, the full article will be retrieved for further evaluation. Challenging decisions regarding the inclusion of an article will be resolved through discussion with the project team. All relevant primary quantitative, qualitative and mixed method studies will be included in the integrative review.

The position statement will be based on the best available evidence, using the hierarchy of evidence provided by the National Health and Medical Research Council (NHMRC). The position statement will be supplemented with references to expert opinion or secondary sources (that is to say, key guidelines, position statements, educational resources, competency and professional standards made by professional societies, associations or organisations). Relevant background articles identified during the search process will be saved separately from included studies for use during the synthesis phase.

Data evaluation

Whilst the importance of using critical appraisal tools to determine the quality of research is widely acknowledged, no "gold standard" tool for assessing the quality of quantitative, qualitative and mixed method research currently exists[17]. As the integrative review will include research from a diverse range of study designs, a critical appraisal tool that assesses a broad range of methodological issues was selected by the project team.

Data evaluation of quantitative, qualitative and mixed method research will be conducted using the Mixed Methods Appraisal Tool (MMAT) which consists of five scoring systems to evaluate the quality of the research studies. This quality appraisal assessment tool was developed from thematic analysis of quality appraisal procedures employed in 17 systematic mixed studies reviews[18]. The MMAT has been validated, pilot-tested and revised to determine separate scoring systems for qualitative, mixed method, randomised controlled, non-randomised and descriptive quantitative studies[17,18]. The MMAT was chosen as the framework to guide the quality assessment process for this integrative review as it provides a systematic, reproducible, descriptive and numerical method of simultaneously critiquing the quality of a diverse range of study designs[18].

The quality appraisal process enables scoring of quality of qualitative, mixed method and quantitative studies in relation to their methodological quality to address the research question. A minimum of two reviewers will independently assess all studies to be included in the integrative review using the MMAT[17]. Any discrepancies will be resolved by consensus or by employing a third independent reviewer. Each reviewer will provide a score

of yes (1), no (0), or not applicable for each of the four listed criteria. The score for all four methodological quality criteria for each domain will be tallied to provide the overall assessment score for each research article[17]. The overall quality appraisal score for each article can be presented numerically or using descriptors, as outlined in the MMAT tutorial[18]. Papers that receive an average score of 75% (quality appraisal score range: 0–100%) will be considered high quality. The relative quality of all included studies will be reported in the integrative review.

Data analysis and synthesis

Data extraction will be completed using the Matrix Method© to enhance the rigour of this stage of the review[19]. This data-extraction method provides a clear framework to systematically extract relevant data from each of the included studies and populate each section of the review matrix. The included studies will be summarised in tabular form and then quality appraised to aid data synthesis. Data from the studies were extracted relating to the research approach, context, sample and key findings. The table headings will include: author (year, country); design; sample; intervention; measures; main findings; limitations; and MMAT score.

To date, integrative review methods for data analysis and synthesis have been poorly articulated and infrequently applied[16]. Consequently, this creates several challenges when combining and synthesising data from a wide range of research designs[16]. Writing an integrative review without a synthesis framework (based on systematic methods) increases the likelihood of error and bias influencing the findings of the review[16]. Thus, the data analysis and synthesis framework plays an integral role, by providing guidance to the author during one of the most difficult aspects of the review — the synthesis of qualitative, quantitative and mixed methods research findings[16]. Ultimately, the chosen synthesis framework should aim to enhance the rigour and accuracy of reporting, as well as reduce bias in the presentation of findings[16]. Once the included studies have been identified, the project team will be able to consider the study designs and select the most suitable synthesis framework.

Ethical considerations

The proposed review will critique and summarise the findings of primary research studies relevant to the topic of interest. Thus, there are no ethical issues of concern.

Discussion

This protocol presents the steps that will be taken to conduct an integrative review of literature, exploring the minimum education and safety requirements for nursing administration of cytotoxic drugs in any setting. The completed review and analysis will inform the development of the CNSA position statement. As the leading organisation for cancer nurses in Australia, CNSA aims to inform nurses about the evidence supporting safety and education requirements for administering cytotoxic drugs, as well as the negative consequences of unsafe practice. The CNSA position statement will be an evidence-based educational resource that outlines the minimum education and safety requirements for nursing administration of cytotoxic drugs. The position statement will also act as an important reference document for health care organisations, providing a summary of current evidence to inform policies and procedures and the provision of a safe workplace environment when administering cytotoxic drugs in any clinical setting. Nurse managers and educators may also use the position statement to guide or update their educational curriculum, ensuring the minimum educational and safety requirements for nursing administration of cytotoxic drugs are met.

The completion of this integrative review of literature will provide current evidence to enable CNSA to achieve its strategic goals of developing and disseminating resources which contribute to advances in cancer nursing practice. The completed body of work (including an integrative review protocol, literature review and position statement) will ensure CNSA takes a leadership role in the provision of evidence to inform cancer nurses about the minimum education and safety requirements when administering cytotoxic drugs in any setting. It is anticipated that this review will identify knowledge gaps in the current literature on this topic and provide direction for future research in this area.

Limitations

There were several limitations for the current review process. The lack of clarity as to the best term to use when referring to drugs administered primarily for the treatment of cancer and have a highly toxic effect on cells, influenced the choice of key words. Both "chemotherapy" and "cytotoxic drug" were used as key terms; however, chemotherapy was the most commonly used term within current studies. The terms for "nurse", "cancer" or "oncology nurse" were used within all articles where the keyword "nurse" was used, providing a clear rationale to refine the list of search terms. The inclusion of different study methodologies enabled a range of research to be explored; however, there was a lack of high-level quantitative research.

Conclusion

This integrative review protocol provides a systematic approach to guide the development of an evidence-based CNSA position statement on the minimum safety and education requirements for the nursing administration of cytotoxic drugs. This protocol will ensure future updates of this document employ a consistent process to provide nurses with up-to-date, evidence-based information over time.

Acknowledgements

This project is funded by the Cancer Nurses Society of Australia.

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Prevalence of high-risk health behaviours in long-term survivors of adult allogeneic blood and marrow transplantation in Sydney, Australia

Gemma Dyer • BN, GradCert Onc, MPH
Northern Clinical School, Faculty of Medicine, University of Sydney, Sydney, NSW, Australia
Blood and Marrow Transplant Network, New South Wales Agency for Clinical Innovation, Sydney, NSW, Australia

Stephen R Larsen • MBBS, PhD, FRACP, FRCPA
Institute of Haematology, Royal Prince Alfred Hospital, NSW, Australia

Nicole Gilroy • BMBS, MAppEpid, MPH, FRACP
Institute of Haematology, Royal Prince Alfred Hospital, NSW, Australia

Lisa Brice • BA, MSS, MPsy, PsyD
Department of Haematology, Royal North Shore Hospital, Sydney, NSW, Australia

Masura Kabir • BSc, MAppSc
Westmead Breast Cancer Institute, Sydney, NSW, Australia

Megan Hogg • BScN, GradCert Onc
Department of Haematology, Westmead Hospital, Sydney, NSW, Australia

Louisa Brown • BN, DipOnc Nursing
Department of Haematology, Calvary Mater, Newcastle, NSW, Australia

Mark Hertzberg • MBBS, PhD, FRACP, FRCPA
Department of Haematology, Prince of Wales Hospital, Sydney, NSW, Australia

Matt Greenwood • BMed, FRACP, FRCPA
Blood and Marrow Transplant Network, New South Wales Agency for Clinical Innovation, Sydney, NSW, Australia
Department of Haematology, Royal North Shore Hospital, Sydney, NSW, Australia
Northern Blood Research Centre, Kolling Institute, University of Sydney, NSW, Australia

John Moore • MBBS, MD, FRACP, FRCPA
Department of Haematology, St Vincent's Hospital, Sydney, NSW, Australia

David Gottlieb • MBBS, PhD, FRACP, FRCPA
Department of Haematology, Westmead Hospital, Sydney, NSW, Australia

Gillian Huang • MD
Department of Haematology, Westmead Hospital, Sydney, NSW, Australia

Jeff Tan • pSc(HIM)(Hon), MPH, MEM
Department of Haematology, St Vincent's Hospital, Sydney, NSW, Australia

Christopher Ward • BMedSc, MBCHB, PhD, FRACP, FRCPA
Blood and Marrow Transplant Network, New South Wales Agency for Clinical Innovation, Sydney, NSW, Australia
Department of Haematology, Royal North Shore Hospital, Sydney, NSW, Australia
Northern Blood Research Centre, Kolling Institute, University of Sydney, NSW, Australia

Ian Kerridge • BA, BMed(Hons), MPhil(Cantab), FRACP, FRCPA
Blood and Marrow Transplant Network, New South Wales Agency for Clinical Innovation, Sydney, NSW, Australia
Department of Haematology, Royal North Shore Hospital, Sydney, NSW, Australia
Northern Blood Research Centre, Kolling Institute, University of Sydney, NSW, Australia

Abstract

Allogeneic blood and marrow transplantation (BMT) survivors are at a significantly increased risk of many preventable conditions that cause long-term morbidity and mortality. The aim of this multi-centre cross-sectional study was to examine Australian BMT survivors and their engagement in high-risk health behaviour known to contribute to these conditions. Of 441 New South Wales (NSW) participants, smoking, drinking more than recommended, being overweight/obese, and inactivity was reported by 7.5%, 12.1%, 48.1%, and 33%, respectively. Rates of "sun-smart" behaviours were high (77%). Time since transplant, lower levels of education and chronic graft-versus-host disease (GVHD) resulted in decreased odds of good health behaviour. Our results suggest that despite well-defined long-term risks, certain subsets of long-term survivors continue to engage in high-risk health behaviours. Therefore, targeted, lifelong counselling and education by nurses about the importance of adhering to preventative health behaviours is critical to improve long-term outcomes.

Keywords: Bone marrow transplant survivors, cancer survivors, health behaviours, high-risk health behaviours.

Please note that the data presented in this manuscript forms part of the Sydney post-bone marrow transplant survey report produced for the the New South Wales Agency for Clinical Innovation (ACI)1.

Introduction

Allogeneic blood and marrow transplantation (BMT) is a lifesaving medical procedure used for the treatment of many malignant and non-malignant diseases in adults and children. With advances in transplantation techniques and supportive care, up to 85% who are alive at two years post-BMT will survive long-term[2]. However, survival is not without consequence. Many long-term survivors experience chronic morbidity, decreased quality of life (QoL) and late non-transplant related mortality. The effects of graft-versus-host disease (GVHD) — a condition in which the donor T-cells recognise the patient as foreign — combined with late toxicities associated with chemo-radiotherapy and immunosuppression, place survivors at a significantly increased risk of many preventable chronic health conditions. Cardiovascular and respiratory disease, diabetes mellitus, osteoporosis, endocrine and gonadal failure, anxiety, depression and secondary cancers all commonly occur after BMT[3], and result in mortality rates four- to nine-fold higher than those observed in an age-adjusted general population for at least 30 years after BMT[4].

According to international consensus guidelines for the long-term care of survivors of allogeneic BMT, primary preventive behaviours should be espoused in an attempt to mitigate this increased risk of poor long-term health[5]. Specifically, these guidelines state survivors of BMT should eat a healthy diet, not smoke, drink alcohol in moderation (<2 drinks per day), maintain a healthy weight, avoid excessive sun exposure and wear sunscreen, and follow age-specific guidelines for physical activity[5] (Australian physical activity recommendations for 18–64 years are at least 150–300 minutes of moderate intensity exercise or 75–150 minutes of vigorous intensity exercise per week, plus at least 2 days per week of muscle-strengthening activities[6]). Early adoption of these modifiable behaviours, it is argued, may help attenuate a subset of the chronic health conditions that survivors experience and improve survivors' QoL[7].

While these guidelines have been available for a decade[8] and campaigns addressing these behaviours have existed in Australia directed at the general population for many years (for example, *Life be in it*[9], *Slip, Slop Slap*[10], *Every cigarette is doing you damage*[11], *Measure up*[12], *Swap it, don't stop it*[13] and *Live Lighter*[14]), it is recognised that behaviour modification can be difficult, even in the context of cancer survivorship. People are familiar with how to prevent morbidity (or prevent further morbidity in the context of allogeneic BMT survivorship), but knowledge does not necessarily result in a desired behaviour[15]. Indeed, while a cancer diagnosis is thought to represent a "teachable moment", many studies have found that despite the increased risks to health, when compared to non-cancer controls, cancer survivors continue to need education and assistance to help change health behaviour in the longer term[16-22].

Although there is a growing body of literature on health behaviours of cancers survivors[23-27], there is a paucity of data on survivors of BMT and no data regarding the health behaviours of Australian BMT survivors. We report the results of a cross-sectional survey of long-term survivors of allogeneic BMT in New South Wales (NSW) to identify their participation in primary preventive health behaviours; to examine the demographic, socio-economic and transplant factors and sequelae associated with lifestyle and health behaviour choices; to identify gaps where cancer nurses are best able to assist this vulnerable and high-risk patient group; and to use this data to support clinical and health policy decision-making for long-term care.

Methods

Patients and procedures

Potential participants were identified from the databases of all adult allogeneic transplant centres in NSW. Participants were eligible if they were ≥18 years of age (at the time of survey) and had undergone an allogeneic BMT at an adult BMT centre between 1 January 2000 and 31 December 2012, were ≥17 years at the time of transplant, could read and write English and could provide consent. Names and phone numbers were provided to the research team. Consenting participants were given the option to self-complete the questionnaire or complete it via a phone interview with one of the researchers. A second round of telephone calls was made to 178 participants who had not returned the survey within a month. No participant elected to be phone-interviewed. All authors had access to primary clinical trial data. The study protocol was approved by the Northern Sydney Local Health District Human Research Ethics Committee (NSLHD Reference: 1207-217M).

Instruments

Engagement in high-risk health behaviours was analysed according to a range of demographic, transplant, psychosocial and lifestyle variables assessed using six survey instruments (five validated and one designed specifically for the study). The five validated instruments included the *Functional Assessment of Cancer Therapy — Bone Marrow Transplant (FACT-BMT Version 4)*[28,29], anxiety stress and depression (*The DASS 21)*[30-32], chronic GVHD (*The Chronic GVHD Activity Assessment — Patient Self Report — Form B)*[33] and *The Lee Chronic GVHD Symptom Scale*[34] and *The Post-Traumatic Growth Inventory score*[35,36].

The sixth survey instrument, the *Sydney Post-BMT Study Survey* was purpose-designed for the study by the research team following literature review and discussion with patients attending BMT late effects clinics — to cover issues not addressed in existing surveys. The survey comprised 402 questions grouped into 20 domains and included questions relating to high-risk health behaviour: smoking, drinking, exercise, diet and body mass index (BMI), and being "sun-smart". ("Sun-smart" behaviour was defined in the survey as "always/routinely wearing sunscreen,

hat, sunglasses, shirts with long sleeves and a collar, and avoiding being in the sun between 11 am and 3 pm".) Other relevant domains included demographics, medical complications, tests and assessments, medications and therapies, infections, vaccinations, complementary therapy use, cancer screening, relationship status, income, and lifestyle factors following allogeneic BMT. The questionnaire used tick-box responses, short-answer questions and five-step Likert scales measuring attitudes and other factors and took approximately one hour to complete. The questionnaire was piloted with BMT survivors to assess face and content validity and to check for comprehension. For each consenting participant, data was collected on dates of diagnosis and transplant, stage/remission status at transplant, transplant conditioning, GVHD prophylaxis, stem cell source and donor type.

Statistical analysis

Categorical responses were summarised using frequencies and percentages. Parametric continuous variables were summarised using means and standard deviations, and non-parametric variables using medians, interquartile ranges (IQR) or ranges. Odds ratios and 95% confidence limits, Pearson chiχ^2 test or Fisher's exact tests were used for comparative analysis of dichotomous categorical variables. Adjusted odds ratios to account for potential confounding effects were determined using multivariable logistic regression analysis. Two sample comparisons of parametric and nonparametric data were determined using the independent t-test, and Wilcoxon Rank Sum tests, respectively; greater than two sample comparisons were determined using one-way Analysis of Variance (ANOVA) and Kruskal Wallis tests. A two-tailed p value <0.05 was used as the level of statistical significance.

Statistical analysis was performed using STATA version 12.1 statistical package (StataCorp, College Station, TX, USA).

Results

A total of 1,475 allogeneic BMT were performed in the study period. Of the 667 recipients known to be alive at study sampling, 581 (87%) were contactable and were sent study packs. Four hundred and forty-one (66% of total eligible, 76% of those contacted) returned the completed survey. Three per cent declined participation (Figure 1).

Of those completing the survey, 250 (57%) were male and 191 (43%) female. The median age of survey respondents was 54 years (range: 19–79). The median age at time of transplant procedure was 49 years (range: 17–71). The median time since BMT was 5 years (range: 1–14) (Table 1)

A range of lifestyle factors were surveyed including smoking, alcohol consumption, weight/BMI, exercise and diet.

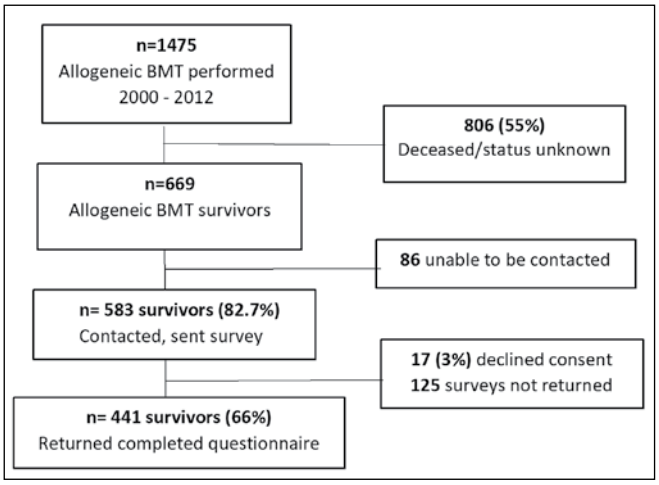

Figure 1: Study flowchart
**Reproduced with permission from the Agency for Clinical Innovation BMT Network Long-Term Follow-Up Group*[1]

Smoking

A total of 33/438 (7.5%) of BMT survivors were smokers — 21/247 (8.5%) males, and 12/191 (6.3%) females. Twelve (36.4%) reported smoking ≤5 cigarettes/day on average; 7 (21.2%) reported 5 to ≤10 cigarettes; and 13 (39.4%) >10 cigarettes per day. One survivor did not report quantity. On univariate analysis factors associated with significantly lower odds of smoking included having some level of university education, having chronic GVHD, and if there had ever been a referral to a respiratory specialist or physiotherapist. There was no significant association between chronic co-morbidities and smoking. The odds of being diabetic and a smoker were lower, though this was not statistically significant.

On multivariate analysis, adjusting for potential confounders, years from date of transplant was associated with increased odds of smoking (OR 1.25; 95% CI 1.08, 1.45; p=0.01) and any level of university education was associated with decreased odds of smoking (OR 0.12; 95% CI 0.03, 0.60; p=0.003).

No measures of personal growth (PTGI), depression stress and anxiety (DASS 21) or QoL demonstrated a significant difference between smokers and non-smokers.

Alcohol

A total of 282/441 (63.9%) of survivors drank alcohol, including 179/250 (71.6%) males, and 103/191 (53.9%) females. Thirty-three (12.1%) of those who drank alcohol reported drinking more than two standard drinks per day on average, (29 male, 4 female). Six (2%) males exceeded four standard drinks per day

On univariate analysis factors associated with significantly lower odds of alcohol use included lower income status and being diabetic. An increased odds of alcohol use was observed in males, those who worked, those with any level of university education and those with mild or no symptoms of GVHD.

Table 1: Demographic, social and clinical characteristics of post-transplant survivors responding to survey (n=441)

Characteristic	Distribution
Socio-demographic	
Gender (Male) n/total (%)	250/441 (57%)
Median age in years (range)	54 (19–79)
Postcode location	
City/inner regional n/total (%)	396/431 (92%)
Income status (A$) n/total responses (%)	
Low income $20,000–$39,999	155/423 (37%)
Middle income $40,000–$79,999	123/423 (29%)
High income >=$80,000	145/423 (34%)
Educational status n/total responses (%)	
Some high school	53/333 (16%)
Completed high school	79/333 (24%)
Trade qualifications/diploma	47/333 (14%)
Some university	24/333 (7%)
Completed university	130/333 (39%)
Transplant factors	
Years since transplant — median (range)	5 (1–14)
Underlying diagnosis n/total responses (%)	
Acute leukaemia	226/423 (53%)
Other *	197/423(47%)
Donor type n/total responses (%)	
Sibling related	250/439 (57%)
Matched unrelated	158/439 (36%)
Haploidentical/mismatched	31/439 (7%)
Conditioning n/total responses (%)	
Myeloablative	214/439 (49%)
Reduced intensity	225/439 (51%)
Post-transplant morbidity and quality of life	
cGVHD	
Total reported cGVHD since transplant n/total responses (%)	301/434 (69%)
Total LEE GVHD score — median (range)	19 (0–77)
Chronic diseases/psychological morbidity n/total responses (%)	
Bone disease (osteopenia, spinal fractures or avascular necrosis)	126/400 (32%)
Cardiovascular risk factors (diabetes, hypertension or elevated cholesterol)	180/414 (43%)
Cancer (mouth, skin, or other)	108/389 (28%)
Anxiety	83/403 (21%)
Depression	95/407 (23%)
Depression, anxiety, stress (DASS 21) — median score (range)	20 (0–118)
Lifestyle n/total responses (%)	
Smoke	33/438 (7%)
Drink alcohol	282/441 (64%)
Exercise/play sport	300/436 (69%)
Always use sun-protection (sunscreen, hat, clothing sunglasses	333/431 (77%)
Median BMI (range) for males	25 (17–63)
Median BMI (range) for females	24 (16–53)
Total FACT BMT — median (range)	110 (32–144)

* CML, CLL, SAA, NHL, HL MM, MDS/Myeloproliferative disease, other (unspecified)

On multivariate analysis adjusting for potential confounders, years from date of transplant was associated with an increased odds of alcohol consumption (OR 1.13; 95% CI 1.01, 1.26; p=0.04) and male gender (OR 2.50; 95% CI 1.18, 5.28; p=0.02).

We further examined associations between alcohol consumption and other measures of personal growth (PTGI), depression stress and anxiety (DASS 21) and QoL. When adjusting for the effects of age, gender and years since transplant, we observed significantly increased odds of improved QoL (FACT BMT score) and alcohol consumption. Significantly lower measures of depression, anxiety and stress were also seen in those consuming alcohol. Comparative measures of personal growth (PTGI scores) were lower in those who consumed alcohol.

"Sun-smart" behaviour

A total of 333/431 (77.3%) of survivors reported sun-smart behaviour, including 192/243 (79.0%) males, and 141/188 (75%) females.

On univariate analysis, those who reported sun-smart behaviour had significantly higher morbidity from GVHD (p=0.03), as measured using the LEE GVHD score. Other factors positively associated with sun-smart behaviours included referral to a dietitian (OR 1.84; 95% CI 0.98, 3.63; p=0.047) and a history of skin cancer (OR 2.39; 95% CI 1.21, 5.07; p=0.008).

On multivariate analysis, no significant associations were observed between socio-demographic variables, co-morbidities, GVHD or referral patterns.

No significant associations were shown between sun-smart behaviours and measures of personal growth (PTGI), depression stress and anxiety (DASS 21) or QoL (FACT BMT), after adjusting for the effects of age, gender and years since transplant.

Weight/BMI

A total of 197/405 (48.6%) of survivors had a normal BMI (≥18.5 to 25), including 103/229 (45.0%) males, and 94/176 (53.4%) females. Thirty-six of those surveyed did not respond to the question on weight and/or height (from which BMI was derived). Thirteen

(3.2%) of survey respondents were underweight (BMI ‹18.5), 128 (31.6%) were overweight (BMI ›25 to ‹30) and 67 (16.5%) were obese (BMI ›30).

On univariate analysis, those with normal BMI had lower odds of diabetes and anxiety.

On multivariate analysis, normal BMI was associated with significantly lower odds of diabetes (OR 0.46; 95% CI 0.23, 0.92; p=0.02) and a trend towards being more years out from the date of the transplant (OR 1.07; 95% CI 1.00, 1.14; p=0.052).

No significant associations were shown between those with normal BMI and measures of personal growth (PTGI), depression stress and anxiety (DASS 21) or QoL (FACT BMT), after adjusting for the effects of age, gender and years since transplant.

Diet

Sixty-five per cent of survivors in the early post-transplant group (‹2 years) reported that their eating habits had returned to normal. In those survivors who were two or more years post-transplant, 77% (292/379) reported that their eating habits had returned to normal.

One hundred and thirty-one survivors reported changing their diet since having a BMT (29.6%). The four most common changes included: avoiding particular food and food groups (37%, n= 48/131), focus on healthy eating (35%, 46/131), reducing meat consumption (16%, 21/131) and choosing organic foods (11%, 14/131). Twelve per cent (52/441) of survivors were taking oral nutritional supplements at the time of the survey.

Physical activity

A total of 300/436 (68.8%) of survivors reported regular exercise post-BMT, including 168/247 (68.0%) males, and 132/189 (69.8%) females.

Two hundred and one (67%) of those who exercised did so at least three times per week.

On univariate analysis, the odds of exercise uptake were significantly lower in those reporting chronic GVHD, hypertension and diabetes. Similarly, referral to a rehabilitation specialist, dietitian or social worker was also associated with lower odds of exercise. An increased odds of exercise was observed in those with no or mild GVHD symptoms

On multivariate analysis, adjusting for potential confounders, diabetes and social worker referral showed a trend towards less exercise, though this association was not statistically significant.

We further examined associations between exercise uptakes and other measures of personal growth (PTGI), depression stress and anxiety (DASS 21) and QoL. When adjusting for the effects of age, gender and years since transplant, we observed that exercise was associated with a significantly better QoL measures (FACT BMT score) and reduced measures of anxiety, depression and stress (DASS 21 scores). No significant association between exercise and personal growth was observed.

Discussion

This study is the first to provide a comprehensive account of high-risk health behaviour in a cohort of long-term survivors of BMT in Australia. Our results reveal that some survivors continue to engage in high-risk health behaviour, despite their increased risks to long-term survival[2,5]. Seven and a half per cent of survivors reported smoking, with nearly 40% of those smoking ›10 cigarettes/day, 12.1% reported drinking ›two standard drinks per day, and almost half had a higher than normal BMI (30% were overweight and almost 17% were obese). Pleasingly, however, 77% reported being "sun-smart", 68.8% were physically active and 35% reported that they had made efforts to eat a healthy diet post-transplant.

In studies of English, Swiss and North American BMT survivors, it was found that when compared to both gender-matched siblings[37] and the general population[38-40], BMT survivors tend to have better health-promoting habits across all health behaviours than comparators with the exception of "active" health behaviours, such as physical activity and eating a healthy diet. When we compare our results to Australian Bureau of Statistics (ABS) data, our survivors also appear to engage less in high-risk health behaviour than the general population[41] (in 2012 the ABS reported that 16% of adults smoked daily, 19.5% of adults consumed ›two standard drinks per day, 62.5% of Australians aged 18 years and over were either overweight (35.3%) or obese (27.5%), only a third were physically active, and 5.1% reported eating the recommended daily amount of fruit and vegetables[37]). However, despite these positive findings, these behaviours do remain concerning, given the significant and pervasive long-term co-morbidities to which BMT survivors are predisposed[42-50].

Our results reveal that time since transplant and being male were significantly associated with smoking and high-risk drinking, whereas higher levels of education, GVHD and referral to a respiratory physician or physiotherapist decreased the odds that a survivor would be a smoker. This is consistent with studies done in other settings, which also reported that younger age at BMT, lower education levels and lack of knowledge of recommendations for post-BMT care are important variables for health behaviours[19,37,39,51,52]. There are several possible explanations for this. Firstly, as the time since BMT increases, survivors generally have less contact with their BMT centres and with other health services, and so may receive fewer reminders about the necessity for adopting and maintaining positive health behaviours. Secondly, as BMT recipients survive beyond the highest risk period (the first two years post-BMT) it is possible that they may begin to believe that they are "in-the-clear" and so free to resume (harmful) pre-BMT behaviour. Importantly, while others have reported that psychological distress is often a trigger for smoking and drinking[53], we found no association

between decreased QoL, depression, anxiety and stress or lower PTGI scores, and, in contrast, found that those who reported drinking alcohol to excess had better QoL and lower depression, anxiety and stress.

While it is reassuring that a high percentage (77.3%) of our survivors reported "sun-smart" behaviours — and that this rate is higher than reported in the Australian general population[54] — there are two important points to stress. The first is that skin cancer in Australia is common; the incidence of melanoma is 11 times that of the average world rate[41]. And the second is that allogeneic BMT further increases the risk of all types of skin cancer due to the long-term use of immunosuppressive drugs, chronic cutaneous GVHD, and the use of azole antifungal agents[55]. Therefore, no amount of sun exposure is acceptable for Australian survivors of BMT. In our study, higher reported GVHD morbidity, a history of skin cancer, and referral to a dietitian were significantly associated with adoption of "sun-smart" behaviour. While it is unsurprising that skin chronic GVHD and previous skin cancer would increase the likelihood that survivors would be more aware of the vulnerability of their skin, the positive association with dietitian referral is less clear, although may simply reflect contact time with health services, and, in particular, with health professionals whose focus is much broader than curing the underlying disease and/or treating the acute side effects of BMT.

At two years post-BMT, a third of survivor reported dietary changes post-BMT — avoiding particular food and food groups, focusing on healthy eating, reducing meat consumption and/or choosing organic foods. The fact that many survivors (77%) returned to their pre-BMT diet, and that only a third had made efforts to improve their nutritional intake is consistent with a recent Japanese, population-based study that was not able to identify differences in nutritional intake between cancer and non-cancer survivors[56]. While this may reflect the complex and intractable nature of eating behaviour, it may also be indicative of the lack of data regarding the impact of diet on chronic non-communicable diseases in cancer survivors and, therefore, both the difficulty that health professionals, and in particular nurses, have in counselling survivors on the most appropriate diet to decrease their long-term health risks, and that survivors have in making dietary choices.

In contrast, regular exercise has been clearly shown to impact QoL, survival and (possibly) cancer progression[17] post-BMT. In our study, 68.8% reported doing some form of exercise. Variables that decreased the odds of exercising included chronic GVHD, hypertension, and referral to a rehabilitation specialist, dietitian or social worker. This data reveals the profound limitations that chronic morbidity, particularly GVHD, which can affect any area of the body, has on survivors of BMT, restricting their mobility and increasing their need for psychosocial support.

Our data reveal that many survivors of BMT appear to be making an effort to maintain their health and wellbeing, compared to the general Australian population. Our results also suggest, however, that given the much greater health risks associated with BMT, much more needs to be done to encourage adoption of positive health behaviours, particularly in certain subsets of survivors. While more research is needed to define the best way to prevent non-communicable disease in survivors of BMT, health-promoting education and support, preferably provided by advanced practice nurses who are uniquely placed to assist cancer survivors, should be rigorously pursued[18].

Despite the large sample size and high response rate (76%) there are a number of limitations to our study that may limit the generalisability of these results to BMT survivors in other countries. Because we relied upon self-reporting and did not capture data on non-responders, we do not know whether BMT survivors who had died prior to study commencement had better or worse engagement with good health behaviour. It is also possible, as with other health surveys, that positive health behaviour may have been over-reported and negative health behaviour under-reported. Another limitation is that we did not ask about pre-BMT behaviour, therefore we are not able to comment on any change in rates of smoking, drinking, BMI or exercise, nor diet type pre- to post-BMT in our survivors. Finally, because only English speakers were eligible to participate in this study, we are not able to comment on other culturally and linguistically diverse (CALD) populations, who may very well have different health knowledge and behaviour.

Conclusion

This study is the largest to explore health behaviours in survivors of BMT in Australia. We found that despite well-defined long-term risks, certain subsets of long-term survivors continue to engage in high-risk behaviours post-BMT, including smoking, drinking alcohol to excess and failing to perform regular exercise. Our results also suggest that adherence to recommendations regarding preventive health behaviours may require ongoing education and counselling and that particular groups of patients — men, those with lower levels of education and those with chronic GVHD, should be the focus of targeted post-BMT nursing education and support.

While the lives of increasing numbers of adults and children are saved by BMT, many survivors bear the burden of chronic and serious illness. While much more research is needed in BMT survivorship and chronic non-communicable diseases to test whether — and which — health behaviour changes make a lasting difference to long-term BMT outcomes, there is no doubt that transplantation clinicians needs to extend their "gaze" beyond the acute phases of transplantation to measures that may prevent, detect and treat modifiable illness in survivors.

Acknowledgements

This research was funded by the New South Wales Agency for Clinical Innovation (ACI), Blood and Marrow Transplant (BMT) Network and supported by the Northern Blood Research Centre. These sponsors are public or non-profit organisations that support health care redesign and medical science in general.

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Two cases presentations of leptomeningeal metastases in the glioma patient

Marina Kastelan • RN, MN (Nurse Practitioner major)
Neuro Oncology Clinical Nurse Consultant, Sydney Neuro Oncology Group, North Shore Private Hospital, Sydney, NSW, Australia
Email: KastelanM@ramsayhealth.com.au

Abstract

Leptomeningeal dissemination of high-grade primary brain tumours remains a challenge to diagnose and treat with a very poor prognosis once drop metastases have occurred. Patient outcomes remain poor, despite some improvement in the overall survival of those diagnosed with glioblastoma; as survival improves, a potential increased incidence of leptomeningeal disease may be seen. However, there has been little improvement in the treatment of leptomeningeal disease over the past 10 years. Nurses must be aware of the unusual signs and symptoms of leptomeningeal disease with the aim of early intervention and patient advocacy.

Background

Leptomeningeal spread, or drop metastases, of glioblastoma occurs when malignant cells travel from a primary location and invade the meningeal tissues of the brain and spinal cord[1,2]. Presentation will be reflective of the site of meningeal deposits; however, this can be ambiguous to diagnose as the patient reports subtle changes or an unusual presentation. Symptomatic leptomeningeal metastases are not common, with few reports documented. Reports vary widely, with some papers suggesting an incidence of between 6% and 21% of spinal seeding from glioblastoma; others suggest much lower numbers, varying between 0.4% and 2%[3-6]. Either way, spinal metastases rarely occur. Whilst seldom seen in the clinical setting, thought mostly to be due to the low survival rates of glioblastoma, leptomeningeal metastases may well become increasingly realised as the local control of primary glioblastoma improves[6,7].

Signs and symptoms of leptomeningeal spread vary between patients and can reflect the site of metastases, but can include any change in mental state, headache, nausea and vomiting, stiff neck, lumbar back pain, leg pain or paraplegia and gait disturbances. They can also include any sign of cranial nerve involvement, presenting as diplopia, facial asymmetry, dysphagia and sensory loss including bowel and bladder dysfunction[1,2,6,8]. Oncology nurses, who may have more repeated, longer and closer interaction with patients and their supports, are in an optimal position to notice subtle neurologic changes, and are then able to advocate for their patients, allowing for earlier intervention, education about symptom management, and psychosocial support.

Glioblastoma, a primary brain tumour, is highly infiltrative and harbours a poor prognosis. In 2016 it was reclassified by the World Health Organization (WHO) as glioblastoma, IDH-wildtype. This latest review by the WHO is a more robust approach to histologically classifying central nervous system tumours using molecular guidelines rather than relying on visual appearance of tumours alone. The recent classification defines a glioblastoma, IDH-wildtype as one that denotes the following features: "predominantly astrocytic differentiation" with atypical nuclear, cellular pleomorphism, mitotic activity, a diffuse growth pattern, microvascular proliferation and/or necrosis; and one which lacks the mutation in the IDH genes[9].

Glioblastoma is the most common primary malignant brain tumour in adults. It accounts for around 50% of all primary malignant brain tumours with a yearly prevalence of around three to four cases per 100,000 population in Australia[9]. There were 1,636 new cases of brain cancer in Australia in 2013, accounting for 1.4% of all new cancers[10]. The incidence of glioblastoma has not increased markedly over the past 20 years; however, the group that has increased in number are those aged greater than 75 years[10,11]. Primary brain cancer is more common in men, with the average age of diagnosis being 64 years[9,11]. Survival remains poor, with most patients dying within 15–18 months of diagnosis[9,15]. Factors associated with a longer survival include a younger age at diagnosis (less than 50 years) and a gross macroscopic tumour resection with no postoperative functional deficits[9]. Overall survival when leptomeningeal involvement is confirmed remains very poor, anywhere from six to eight weeks to six months[1,8].

The presenting signs and symptoms for those with primary brain tumours vary and depend on the "size, location, compression or infiltration of cerebral tissue, related cerebral oedema and the development of raised intracranial pressure"[12]. The signs and

symptoms of raised intracranial pressure (ICP) include headache (usually worse in the morning and may increase in severity with coughing, straining and bending), nausea and vomiting, seizures, focal neurological signs and decreased levels of consciousness[13]. However, patients with primary brain tumours may not present with these symptoms but rather more subtle neurological changes in speech, vision, strength, memory or mood[12].

Diagnostic workup

The most accurate imaging for the diagnosis of drop metastases is magnetic resonance imaging (MRI) with gadolinium. Cerebrospinal fluid (CSF) cytology collected via lumbar puncture can also be assessed but has poor sensitivity and is not always representative of the presentation history[14]. Furthermore, assessment of the CSF cytology has a high false-negative proportion, with estimates of only 50–70% showing evidence of malignant cells[1,8]. Therefore, multiple CSF collections are recommended. Additionally, as some leptomeningeal disease presents as scattered pial dissemination, with the appearance of "salt and pepper" rather than bulky enhancement, MRI with gadolinium may not reflect the clinical picture. MRI has a sensitivity of around 70% for diagnosing leptomeningeal metastases, so leptomeningeal disease may need to be suspected, rather than confirmed, providing this is combined with an assessment of the patient's related symptoms and combined clinical picture[8].

Prognosis

Prognosis for patients with leptomeningeal metastases is extremely poor due to the diffuse nature of the disease. The treatment therefore is palliative, with an emphasis on symptom control[2,6,8].

The purpose of the following two case presentations is to illustrate the challenges in diagnosis and treatment of patients with drop metastases, given the uncommon and often variable symptoms at initial presentation. Each of these patients presented in a different way with unusual progression of the tumour.

Case presentations

Patient One

AB is a 46-year-old male with a known history of left temporo-occipital glioblastoma, IDH-wildtype, diagnosed 16 months prior. He had previously undergone standard treatment for glioblastoma, including a craniotomy (with gross total resection of the tumour achieved) followed by concurrent chemoradiation (with oral temozolomide) for six weeks then adjuvant temozolomide (commencing at 150 mg/m^2 then increasing to 200 mg/m^2) five days per month for six months, as per current guidelines[15]. He had initially presented after a seizure. He had been on eight-weekly MRI surveillance and had been reviewed in the outpatient setting on a four-weekly basis.

AB's wife called to report changes in her husband. He had been getting up at night unable to sleep because of discomfort in his lower back. He also had suddenly developed a left-sided facial droop with left eye droop. Upon further questioning, he had no headache, no nausea or vomiting and reported no new seizures. His only medication was oral phenytoin 400 mg daily. The patient's wife reported that he had experienced some neck pain one week earlier which had resolved.

It is acknowledged that leptomeningeal spread is not often seen, as patients do not survive long enough to develop metastases. The most common sites for leptomeningeal disease to occur are the lower thoracic, upper lumbar and lumbosacral spine, most likely due to gravity, where the patient presents with lower back pain[7,14]. Simply, leptomeningeal disease ensues once tumour cells move from the primary site and infiltrate the meningeal membranes, travelling freely within the CSF to any structure in contact with the CSF[1,7].

Mr AB underwent a whole spine MRI, which confirmed subtle leptomeningeal enhancing deposits surrounding the conus and involving the cauda equina nerve roots. The report noted that there was "thickening and enhancement of the cranial nerves VI, VII and VIII, nodular leptomeningeal deposits surrounding the conus and involving the cauda equina nerve roots". Cranial nerve VII, the facial cranial nerve, accounts for the taste at the front of the tongue, tears, saliva and muscles of facial expression, thus the associated facial droop.

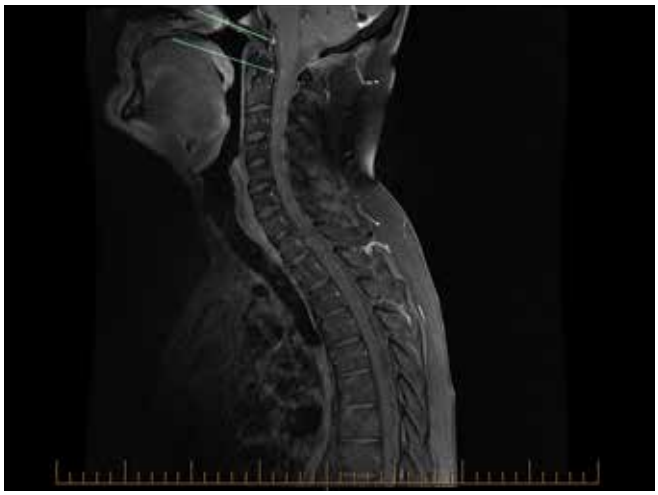

Figure 1: MRI spine sagittal T1 with contrast showing bulky deposits along the cranial nerves VI, VII and VIII

The conus or conus medullaris is the area where the spinal cord becomes tapered where it reaches the lower two-thirds of the thoracic region[12]. As the spinal cord is shorter than the vertebral column, the "lumbar and sacral spinal nerves develop long roots, collectively known as the cauda equina"[12].

Due to the rare incidence of leptomeningeal metastasis, there are no published guidelines for their management, nor an effective treatment. Prognosis is usually poor. Treatment goals

are to achieve symptom control but it is acknowledged this will not improve neurological symptoms[7]. Surgical intervention for leptomeningeal disease (either for resection or histopathological confirmation) is not recommended due to the pial or "salt and pepper" nature of the disease. Treatment is focused on reducing the tumour burden with chemotherapy, radiation or stereotactic radiation[1].

AB was commenced on analgesia including oxycontin, pregabalin and endone as required to optimise pain relief. He was referred to radiation oncology for consultation and consideration of radiotherapy to the spinal lesions.

The management for patients with glioblastoma is multifactorial and best undertaken by a multidisciplinary team with expertise in the disease. Nurses, acting as an advocate and who frequently offer therapeutic contact as part of the continuum of care process, may positively affect quality of life in this patient group.

Treatment for each patient is individualised. With isolated leptomeningeal spread, the aim of external beam radiotherapy is to control pain and prevent further disease progression or delay symptomatic progression. Most patients with leptomeningeal spread usually have multifocal or pial involvement with a very poor prognosis, hence surgical intervention is not usually an option. Prompt referral to palliative care services is essential to maximise symptom control and quality of life.

AB received 10 fractions of palliative radiation, and died 15 weeks after the diagnosis of leptomeningeal metastases.

Patient Two

DC is a 55-year-old male who initially presented with headaches and vomiting and was found to have a space-occupying lesion in the right temporal lobe. He underwent a gross total resection of the right temporal lobe tumour with histology confirming a glioblastoma, IDH-wildtype. He was well postoperatively with no deficits. DC then received standard treatment according to current guidelines, comprising six weeks of combined chemoradiation (with concurrent temozolomide) followed by adjuvant temozolomide for five consecutive days each month for six months[15].

Throughout the treatment trajectory he had visited his general practitioner (GP) complaining of left shoulder pain. An MRI of his shoulder reported a labral tear and the patient was referred to an orthopaedic surgeon and a physiotherapist. He also reported a one-week history of abdominal pain. A computed tomography scan (CT) of his chest, abdomen and pelvis was reported as "no abnormalities detected". Furthermore, the patient reported a week's history of right groin and testicular pain. A scrotal ultrasound was reported as "no abnormalities seen". A urine microsensitivity and culture returned a negative result.

The patient then presented for a surveillance MRI and review in the oncology outpatient clinic complaining of ongoing shoulder and groin pain. An MRI of his whole spine was arranged. The common presenting symptoms of drop metastases to the spinal cord are back pain, nerve root pain and limb weakness, which may progress to para or quadriplegia[14].

DC was found to have a 7 mm enhancing nodule between the nerve roots at the third and fourth lumbar (L3/4) level, abnormal enhancement in the sacral canal at the third sacral (S3) nerve and related to the first sacral (S1) nerve root. All findings were consistent with drop metastases. Furthermore, there was a 6 mm nodule at the fifth and sixth cervical (C5/6) region, which appeared to extend into the exit foramen. This progression with

Figure 2: MRI spine sagittal T1 with contrast showing C 5/6, T3/4 and T9 drop metastases

Figure 3: Thoracic spine T8 and 9 drop metastases

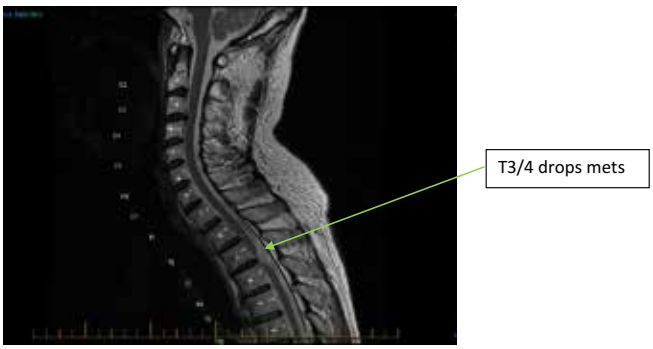

Figure 4: Thoracic spine T3/4 drops metastases

drop metastases occurred just over six months after his initial treatment.

DC's symptoms were optimised with analgesia including pregabalin and targin (oxycodone hydrochloride and naloxone hydrochloride). He was referred to the palliative care team for ongoing pain management and end-of-life support. He was referred to the radiation oncology team and completed further radiotherapy to the spinal leptomeningeal metastases, aiming to halt disease progression and maximise pain control.

DC went on to have further spinal imaging eight weeks after initial spinal radiation. Unfortunately he was found to have progression of the pial metastatic lesions as well as compression and displacement of the spinal cord at the third and fourth thoracic vertebrae. The treatment plan included further radiation to these vertebrae. DC remains alive at this report and surprisingly mobile and able to carry out his usual activities of daily living.

Conclusion

Leptomeningeal spread of a glioblastoma is rarely seen in the clinical setting; however, it may become a greater issue for patients as treatment for glioblastoma improves. Treatment of leptomeningeal drop metastasis remains a challenge for all clinicians, offering little improvement or control of this disease.

Acknowledgement

The author would like to thank Jeanne Barr, Neurosurgical Clinical Nurse Consultant, Royal North Shore Hospital, for her support with the writing of this paper.

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Venous access practices for delivery of chemotherapy for women with breast cancer

Alison Szwajcer • MSc (Nursing), BN, Onc Cert
Clinical Nurse Consultant, Cancer Care Centre, St George Hospital, Kogarah, NSW 2217, Australia

Rosemary Hannan • Nursing Cert, Onc Cert
Breast Cancer Nursing Cert, Clinical Nurse Consultant, Cancer Care Centre, St George Hospital, Kogarah, NSW 2217, Australia

Liane O'Brien • BAppSc (Physiotherapy)
Senior Physiotherapist, St George Hospital, Kogarah, NSW 2217, Australia

Marie Fournaris • BAppSc (Occupational Therapy)
Senior Occupational Therapist, St George Hospital, Kogarah, NSW 2217, Australia

Prof Ritin Fernandez • Phd, MN, BN
Professor of Nursing, Centre for Research in Nursing and Health, St George Hospital, School of Nursing, Midwifery and Indigenous Health, University of Wollongong, St George Hospital, Kogarah, NSW 2217, Australia

* Corresponding author

Abstract

Purpose To explore venous access practices for delivery of chemotherapy for women with breast cancer.

Method Medical records of all women (N=274) who had breast cancer surgery and who received chemotherapy for breast cancer over a three-year period were reviewed.

Findings One hundred and fifty seven (57%) of women required 16 or more chemotherapy treatments and of these women 83 (52%) required a central vascular access device (CVAD). Fifty-four (34%) had a CVAD inserted prior to chemotherapy whilst the other 29 (18%) had one inserted after commencing chemotherapy. Women who received only four cycles of chemotherapy did not require a CVAD.

Conclusion Venous access needs to be considered for women having chemotherapy for breast cancer as over half of women who have a longer duration of chemotherapy will require a CVAD. There is no definitive answer as to whether women who have a sentinel node biopsy can be cannulated on that arm.

Introduction

Appropriate venous access remains the quintessence for the management of patients receiving intravenous chemotherapy[1]. In addition, venous access is also required for these patients as they require frequent pathology whilst receiving chemotherapy[2]. In the clinical setting, the common option to obtain venous access is by inserting a peripheral cannula; however, for many patients receiving chemotherapy, peripheral cannulation remains difficult[3]. Reasons for difficult cannulations include poor veins, anxiety, dehydration and inexperienced staff[4]. Having experienced staff who are aware of both the physical and the psychological aspect of ongoing cannulations can help to minimise the discomfort for the women. Preservation of veins is important as patients may require unrelated treatment necessitating venous cannulation.

Other options to obtain venous access include insertion of a central vascular access device (CVAD) including implantable devices such as portacaths, and peripherally inserted central catheter (PICC) lines[3]. These devices are being increasingly recommended in order to reduce the number of peripheral cannulation attempts in patients requiring intravenous medications for an extended period of time[2]. The advantages of using CVADs include increased patient comfort[4], obtaining blood samples and administering intravenous antibiotics when required. Although CVADs have their advantages, there are also complications associated with them. CVADs remain a leading cause of nosocomial infections[5] for patients receiving chemotherapy as these patients are often immunocompromised[6]. Other complications associated with CVADs include thrombosis, catheter malfunction and catheter fracture[7]. The selection of the venous access device is largely dependent upon the type of chemotherapy, duration of access, quality of veins, patient preference and physician factors[6].

Breast cancer is the most frequently occurring cancer in the world for women, accounting for 25% of all cancers[8]. For women with breast cancer, there are additional concerns associated with venous access depending on the type of surgery. Having an axillary lymph node dissection (ALND) increases the

potential for the development of restricted arm movement, pain and lymphoedema[9]. The incidence of lymphoedema following axillary surgery for breast cancer has been reported to be up to 42%[10] and the risk of developing lymphoedema increases according to the number of lymph nodes removed[11]. Due to the potential risk of developing lymphoedema of the arm, obtaining venous access on the affected side has traditionally been strongly discouraged[12]. This limits the options for the health professional as cannulation can only be performed on the unaffected arm.

It has been well established that more than 70% of women with early breast cancer have no evidence of axillary node metastases therefore ALND is not necessary[13]. For these women, sentinel node biopsy (SNB) is a more precise surgical technique that is extensively used for determining the extent of the spread of the cancer to the lymph nodes[14]. Benefits of SNB include less arm morbidity, particularly a decrease in the loss of sensation, and reduced shoulder abduction range of motion[14,15]. In addition, there is decreased pain in the affected arm and lower risk of lymphoedema[14,16].

To prevent compromising the lymphatic drainage of the arm following breast surgery and SNB, most hospitals recommend not using the affected arm for venous access[17]. There is limited literature investigating the current venous access practice for delivery of chemotherapy for women with breast cancer. The aim of this study was to investigate the venous access practices for delivery of chemotherapy for women with breast cancer.

Methods

Study design

A retrospective audit of the medical records was conducted for women who had breast cancer surgery and who received chemotherapy for breast cancer over a three-year period.

Setting

This study was conducted at three metropolitan hospitals (two public and one private hospital) in New South Wales (NSW) Australia.

Inclusion and exclusion criteria

Women who met the following inclusion criteria had their medical records reviewed: (1) surgery that included either a sentinel node biopsy or an axillary clearance for breast cancer; and who (2) received chemotherapy at one of the three participating hospitals. The medical records of women who did not have either a sentinel node biopsy or an axillary clearance or chemotherapy were excluded.

Data collection

Data was collected relating to: (a) participant demographics including age and medical record number; (b) the surgical procedure including the date of surgery, type of surgery to the breast, type of axillary surgery, number of surgeries undertaken; (c) the chemotherapy treatment including the chemotherapy regimen and the total number of treatments the woman received; (d) venous access including the type of venous access used during the treatment regimen, the number of cannulations required for each chemotherapy treatment and the site of cannulation; (e) incidence of lymphoedema (self-reported and objectively assessed by arm measurements in the lymphoedema clinic); and (f) incidence of hospital admissions for chemotherapy-related side effects.

Information was gathered for the audit by one of the members of the research team from a number of different sources. These sources included the participants' paper notes, the hospitals' central patient record database, the local databases used in the Division of Cancer Services and the Breast Cancer Service, and the Lymphoedema Service files. The medical record number was used as the unique identifier to match patients within each database. Ethics approval to conduct the study was obtained from the Human Research Ethics Committee of the participating hospitals.

Data analysis

Data from electronic records were exported into an Excel database. Data was de-identified by an assistant not associated with the project and imported into SPSS Version 17 for analysis. A random audit of 5% of participants was also performed by the assistant to review the integrity of the data. The number of cannulations required for each woman was calculated according to the chemotherapy regimen prescribed. For example, if a woman was prescribed four cycles of chemotherapy, she would require four cannulas. Descriptive statistics including frequencies and percentages are used to present the data. Differences in incidence of lymphoedema were assessed using the chi-squared test. Results were considered to be statistically significant if results were $p<0.05$

Results

Data were collected from the medical records of 274 women. The mean age of the women in the study was 51.7+/- 10.3 (range 29–77 years). Almost two-thirds (63%) of the women (n=173) were aged between 40 and 59 years.

One hundred and seventy three women had only one axillary surgery, 101 required a second axillary surgery. The initial surgery for 158 women was a sentinel node biopsy and the remaining women (n=109) had an ALND. Of the 101 women who required a second axillary surgery, four had an SNB and 32 had an ALND. Overall, SNB and ALND were performed on 133 and 141 women, respectively

The chemotherapy regimens included Adriamycin and Cyclophosphamide (A/C) with or without Paclitaxel, with or without Trastuzumab; Fluorouracil, Epirubicin and

Cyclophosphamide (FEC) with or without Docetacel; Docetaxel, Adriamycin and Cyclophosphamide (TAC); Docetaxel, Cyclophosphamide, Trastuzumab (TCH); and Docetaxel, Carboplatin (T/C). The total number of chemotherapy treatments ranged from 4 to 29 cycles.

Table 1: Baseline demographic and medical characteristics of participants (n=274)

Characteristics	N	%
Age at diagnosis		
20–39 years	36	13.1
40–59 years	173	63.2
60–79 years	65	23.7
Number of women with		
Axillary clearance	141	51.5
Sentinel node biopsy only	133	48.5

All peripheral venous cannulas were inserted by a registered nurse. Seventy-six per cent of the women (n=209) received their first chemotherapy regimen through a peripheral cannula. Thirty-nine of the 209 women (19%) had a CVAD inserted prior to commencing the second chemotherapy cycle. A total of 170 women received their chemotherapy regimen through peripheral cannulas throughout their treatment.

The number of cannulations that women received depended on their chemotherapy regimen and varied from four to 29. Sixty one per cent of women received the exact number of cannulas according to the chemotherapy regimen. Twenty-seven per cent of women required an extra one or two cannulations, whilst 12% of the women received between three and eight additional cannulas. Thirty-eight women (14%) had peripheral cannulas inserted at least once on the affected side.

The overall incidence of lymphoedema was 20.8% (n=57). The percentage of women who developed lymphoedema was significantly greater in those that had an axillary clearance (n=42) compared to those that had a sentinel node biopsy (n=15) (P=0.0003). Of the 57 women who had lymphoedema, 18 (32%) had a CVAD and 39 (68%) had peripheral cannulas inserted during their treatment. None of the CVADs were inserted on the affected arm; however, three peripheral cannulas were inserted on the affected arm, all in women who underwent an ALND.

Eighty (29%) women were admitted to hospital whilst they were having chemotherapy, with the length of stay ranging from 1 day to 13 days (mean of 5 days (SD 3.09)). Of these women, 12 (4%) had a second admission and 5 (2%) were admitted thrice. Of those admitted, 42.5% (n=34) had blood taken from a CVAD whilst the remaining (n=46) did not have a CVAD and so had peripheral venepunctures for blood tests. The number of times blood was taken from the 80 women during hospital admissions ranged from 1 to 17 with a mean of 5 (SD 3.309).

Discussion and implications for further research

Chemotherapy is an integral part of the management of breast cancer. This study was undertaken to investigate the venous access practices among nurses for delivery of chemotherapy for women with breast cancer in three metropolitan hospitals. Over half of the women (51.5%) had chemotherapy following an ALND; therefore, generalisation of these results to those women

Table 2: Chemotherapy treatments

Number of chemotherapy cycles	Chemotherapy regimes	Total number of peripheral cannulas anticipated	Number of women requiring CVADs	Number of women	Axillary lymph node clearance	Sentinel node biopsy
4–6 cycles	A/C x 4, TAC x 6, FEC x 6 FEC x 3 + Docetaxel x 3 T/C x 4	4 6 6 6 4	21	116 (42%)	2 (0.72%) 18 (6.56%) 0 (0%) 11 (4.01%) 13 (4.74%)	22 (8.02%) 0 (0%) 16 (5.83%) 7 (2.55%) 29 (10.58%)
7–16 cycles	A/C x 4 + Paclitaxel x 12 weeks A/C x 4 + Docetaxel x 4 (1 patient)	16 8	41	90 (33%)	63 (22.99%) 1 (0.36%)	24 (8.75%) 0 (0%)
>17 cycles	A/C x 4 + Paclitaxel x 12 weeks + Herceptin TCH + Herceptin Paclitaxel + Herceptin	29 17 25	42	68 (25%)	24 (8.75%) 10 (3.64%)	19 (6.93%) 14 (5.10%)

who had axillary surgery in general should be undertaken with caution.

The results of this study demonstrate that women will require between four and 29 peripheral cannulas for their chemotherapy treatment depending on the particular regimen. In addition, the introduction of targeted therapy has extended the treatment duration for some women up to 14 months, which has implications for the choice of venous access.

Seventy-six per cent (n=209) of the women had their first chemotherapy through a peripheral cannula. This could be due to various reasons. Firstly, these women could have had aggressive breast cancer, requiring expedited commencement of chemotherapy according to recommended evidence-based guidelines. Due to the limited resources available it could be plausible that there was limited availability of personnel to insert the CVAD, hence peripheral cannulas were initially used to prevent delaying the commencement of chemotherapy.

Secondly, the women may have declined the option for having chemotherapy using a CVAD. Finally, venous assessment may not have been undertaken prior to the women starting their chemotherapy treatment. This result has implications for nurses in terms of using validated venous access selection tools to guide their choice of either peripheral cannulas or CVADs. During the course of chemotherapy the number of CVADs increased, which could be due to difficulties with cannulation.

The study showed that almost 40% of the women required more than the anticipated number of cannulas. Various reasons can be postulated for this result. It could be possible that due to effects of chemotherapy drugs there can be phlebitis, causing difficulties with peripheral cannula insertion. In addition, the choice of veins can become more limited due to thrombosis, associated with ongoing chemotherapy[18]. It could also be plausible that due to staff shortages and more junior staff there were a limited number of nurses with skills in inserting peripheral cannulas.

These results have implications for nursing practice. Firstly, it is vital that nurses provide education to women prior to commencing chemotherapy about peripheral cannulas and CVADs. Patient education and their participation in appropriate device selection remains paramount in decision making in order to ensure successful completion of treatment. Secondly, it ensures there is the provision of adequate resources to help women to make their choice.

The overall incidence of lymphoedema was 20.8%. This high result could be due to the fact that subjective assessment of lymphoedema was undertaken in some of the women. Only five of the 38 women who had an SNB or ALND and were cannulated on the affected arm developed lymphoedema. This result could be related to other factors such as arm mobility, postoperative wound infection, radiotherapy to the axilla or an increased body mass index as these can also contribute to the development of lymphoedema[19].

Whilst there is limited literature about cannulation of the affected arm and venepuncture following an SNB, the results raise some important points. Current clinical practice dictates that the arm on the affected side should be avoided for cannulas[12] due to the increased risk of breast cancer-related lymphoedema. In this study, 11% of the women who had an SNB and 29% of the women who had an ALND developed lymphoedema. This result relating to women with ALND is congruent with the evidence found in the literature. However, in this study the incidence of lymphoedema among women who had an SNB was 11.2%, which is high when compared to the literature which reports 5%[14,16]. These results have implications for cannulation practices in women who have had an SNB. Until further rigorous research is available, cannulation on the affected arm should be avoided in women having an SNB.

The major strength of this study was that it was a multicentre study incorporating data from three different hospitals. In addition, the sample size involving 274 women enables the generalisability of the findings to patients with breast cancer requiring chemotherapy in metropolitan hospitals. Further research needs to be undertaken on cannulation practices in women receiving chemotherapy in rural and regional areas.

Despite the strengths of the study, some limitations inherent in undertaking retrospective research need to be acknowledged.

Table 3: Number of women who had a CVAD

Number of chemotherapy treatments	CVAD prior to first chemotherapy	CVAD after first chemotherapy	No CVAD during chemotherapy
4–6 116 women	11 (9.5%)	10 (8.5%)	95 (82%)
7–16 90 women	22 (24.5%)	19 (21%)	49 (54.5%)
17–29 68 women	32 (47%)	10 (15%)	26 (38%)
Total	65 (24%)	39 (14%)	170 (62%)

Firstly, the number of women who developed lymphoedema could be underestimated given that women could have received treatment elsewhere for the lymphoedema. It was beyond the scope of this study to identify these women. Another limitation of the study was that the number of peripheral cannulation procedures required if a woman was admitted to hospital while receiving chemotherapy was not collected. Future studies should take this into consideration as admissions to hospital require regular blood tests, and insertion and replacement of IV cannulas have an impact on the venous access for patients.

Further research assessing the effects of various cannulation assessment tools in the future is warranted.

Conclusion

The results provide an understanding of the cannulation practices used for gaining venous access in women having chemotherapy following axillary surgery for breast cancer. It appears that women who have an SNB can be at increased risk of breast cancer-related lymphoedema when cannulated on the affected arm.

Implications for nursing

The results of this study indicate that cannulation of the affected arm should be avoided in women having axillary surgery. However, until further rigorous research is available, the practice of cannulation for women following axillary surgery will be dictated by hospital policy and protocols. Assessing appropriate venous access devices for women having chemotherapy for breast cancer is important for uncomplicated administration and prevention of complications.

Knowledge translation

- Venous access for women receiving long-term adjuvant chemotherapy for breast cancer was mainly undertaken using a CVAD.
- Assessing appropriate venous access devices for women having chemotherapy for breast cancer is important for uncomplicated administration.
- Nurses should be aware of the risk of developing lymphoedema after a sentinel node biopsy when cannulating on the affected arm.

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Christine was the inaugural nursing recipient to be awarded the Wilbert E. Fordyce Clinical Investigator Award and in 2010, the American Cancer Society Clinical Research Professorship. In 2015, she was inducted into Sigma Theta Tau International Researcher Hall of Fame. Currently, Prof Miaskowski's research team have funding worth over $50 million (US) to conduct research across a broad range of areas, including symptom management, pain management, symptom clusters, genetics, epigenetics and more. Prof Miaskowski has published close to 500 refereed publications, principally published in the top-ranking Nursing and Oncology journals.

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