National Child Cancer Network NZ

Linking care /
Sharing knowledge /
Advancing best practice /

Adolescent and Young Adult Malignant Bone Tumour Survival in New Zealand 2000 - 2009: A retrospective chart review

Preliminary Report
prepared by

Kirsten Ballantine
for the

AYA Information Gaps Working Group
AYA Cancer Network Aotearoa

June 2015

Contents

Study Background and Aims

This current project follows on from a study titled *'Adolescent and Young Adult Cancer Incidence and Survival in New Zealand 2000-2009'* which was prepared for the AYA Advisory Group and released by the Ministry of Health in December 2013. The AYA cancer incidence and outcomes study utilised New Zealand Cancer Registry (NZCR) data to report cancer incidence and survival for New Zealand AYA aged 15-24 years.

A key finding from this analysis was that New Zealand survival rates for AYA diagnosed with malignant bone sarcomas were well below international benchmarks. For example, five-year relative survival for adolescents (15-19 years) was 46%, considerably poorer than the survival rates for adolescent malignant bone tumours reported by the United States (63%), Scotland (67%), and Canada (68%). AYA bone tumour 5-year relative survival was also lower for Maori AYA (37%) compared with non-Maori/Pacific Peoples (53%). A subsequent analysis of the 25-29 year cohort, showed similarly poor survival outcomes; 5-year survival was half the 66% survival probability achieved by Australia within a similar time period.

It was clear that further in-depth analyses were required in order to identify the potential causes of our AYA bone tumour survival disparities and highlight potential areas of improvement to the future service delivery for this group. However, the data fields routinely collected by the NZCR are necessarily limited, and therefore any potential contributing factors could not be determined from registry data alone. A retrospective chart review was therefore undertaken to retrieve data pertaining to onset of symptoms, presentation, histology, site, disease staging at diagnosis, chemotherapy, radiotherapy, clinical trial participation, surgery, disease recurrence, secondary malignancies, and cause of death.

The purpose of this preliminary report is to;

- Generate discussion around the findings to date
- Identify additional hypotheses which are able to be tested through this dataset
- Inform decisions around future research directions
- Plan the dissemination of the key study findings

This summary has been prepared exclusively for the AYA Information Gaps Working Group and clinicians who have been directly involved with the study.

Due to the small number of bone tumour cases diagnosed annually among AYA in New Zealand and the study limitations described at the end of this report, any between-group differences should be interpreted cautiously.

Project Timeline

March 2013: The provisional findings from the *'Adolescent and Young Adult Cancer Incidence and Survival in New Zealand 2000-2009'* analysis are presented to the AYA Advisory Group. A key finding is that survival rates for AYA diagnosed with malignant bone tumours are well below international benchmarks and are particularly poor for Maori.

April 2013: Dr Mark Winstanley and Dr Mandy PohLui De Silva undertake to complete a retrospective chart review in order to examine a range of variables which may have contributed to New Zealand's poorer survival rates.

July 2013: Following discussions between Dr Ruth Spearing and Dr Mark Winstanley, a research proposal for a University of Otago Summer Studentship is submitted in order to fund a medical student to complete a review of the South Island AYA bone tumour cases. The project is supervised by Dr Rob Corbett, Dr Ruth Spearing, Mr Gordon Beadel, Kirsten Ballantine, and John Carson. It is funded by the Ruth Spearing Cancer Trust, with additional financial support from the Children's Cancer Research Trust.

October 2013: The summer studentship to review the South Island bone tumour cases is undertaken by Angela Zhang, a fourth year medical student. Upon completion of the South Island review, Angela also begins reviewing the North Island cases, as Mandy PohLui De Silva is no longer able to commence the project ahead of going on maternity leave. Angela prepares a brief report based on the cases reviewed to date (63/122) in fulfilment of the Summer Studentship requirements.

July 2014: The AYA Cancer Network establishes the AYA Information Gaps Working Group. The group, lead by Dr George Laking, undertakes to seek funding to complete the bone tumour review which is subsequently provided by the Children's Cancer Research Trust.

October 2014: Sarah Dawes, Clinical Trials Coordinator, Cancer Trials NZ is appointed to a fixed term position in order to complete the North Island case review.

December 2014: Sarah Dawes' fixed term contract comes to an end. Most case reviews have been completed but some remain outstanding due to difficulties obtaining locality authorisation and requesting notes from some DHBs.

March 2015: Kirsten Ballantine completes the remaining case reviews and commences conducting the preliminary analyses.

June 2015: The preliminary report is prepared for members of the AYA Information Gaps Working Group and co-supervisors of the University of Otago Summer Studentship Project.

Methods

The clinical records of 122 AYA (15-29 years) diagnosed with a malignant bone tumour as reported to the NZCR within the period between January 2000 and December 2009 were reviewed. Three cases were subsequently excluded from the analysis; one because the case was informed to the NZCR by death certificate only, one because there were so many gaps in the data, and one because the medical records for the deceased patient had already been destroyed. This resulted in a final dataset of 119 cases.

It should be noted that there will be subtle differences between the figures reported below and those from the original analysis. This is due to the exclusion of the 3 cases noted above, the reporting of observed survival as opposed to relative survival, the extension of the follow-up period to 31st December 2013, and the reporting of survival for the entire follow-up period rather than focusing on five year survival. These are not considered substantial changes, as deaths among the general AYA population are rare and only one patient died more than five years post diagnosis. All deaths that occurred within this cohort were directly attributable to their disease.

Data collected from the clinical records included the following variables:

DEMOGRAPHICS	
NHI	Date of birth
Gender	Date of death
Ethnicity	Cause of death
Residence	Residence at diagnosis
DIAGNOSIS	
Date of symptom onset	Diagnosis sub classification
Symptoms	Diagnosis site
Date of presentation to tertiary care	Staging at diagnosis (localised / metastatic)
Date of histological diagnosis	Site(s) of metastases
Diagnosis	Relevant medical history
TREATMENT CENTRE	
Centre of diagnosis	Multi vs single centre
Referral process	Other treatment centre(s)
Treatment centre	Treated in adult vs paediatric oncology
TREATMENT PROTOCOL & CHEMOTHERAPY	
Enrolled in a clinical trial	Treatment protocol followed
Reason why not enrolled in a clinical trial	Completion of protocol
Chemotherapy received	Chemotherapy end date
Chemotherapy start date	
SURGERY & RADIOTHERAPY	
Date of surgery	Histological necrosis
Surgical centre	Surgical reconstruction
Surgeon	Wound complications
Resection margins	Date of complication resolution
Volume of primary tumour	Radiation start date
Radiation doses	Radiation sites
DISEASE RECURRENCE & SECOND MALIGNANCIES	
Recurrence post therapy	Recurrence date
Recurrence site	Second site
Second malignancy	

Demographics

Although bone tumours are more common in the AYA age bracket than in the very old or very young, nevertheless only around 12 young people between the age of 15 and 29 are diagnosed with a bone tumour in New Zealand each year.

Of the 119 patients in this cohort, 56 (47%) were diagnosed with a Ewing sarcoma and 51 (45%) with osteosarcoma. The remaining 10 patients (8%) were diagnosed with another chondrosarcoma (7), chordoma (2) and an undifferentiated sarcoma of the bone (1).

Overall bone tumour survival was 45.4%, . Median survival for bone tumours was 16 months. Median survival for those with Ewing tumours was 15 months (range: 3 months – 8½ years) and 21 months for those with osteosarcoma (range: 6 months – 4¼ years). Survival for the ten AYA diagnosed with other types of bone tumours was higher at 60%. However, 3 out of those 4 patients who died did so within three months of diagnosis.

Fewer females AYA were diagnosed with bone sarcomas than males and their survival was higher for both osteosarcoma and Ewing tumours.

	TOTAL BONE TUMOURS		**TUMOUR GROUP**					
			Ewing tumour		**Osteosarcoma**		**Other bone tumour**	
	n	**observed survival (%)**	**n**	**observed survival (%)**	**n**	**observed survival (%)**	**n**	**observed survival (%)**
Sex								
Male	74	41.9	32	31.3	35	42.7	7	71.4
Female	45	51.1	24	50.0	18	55.6	5	33.3
Age group								
15-19	81	46.9	39	43.6	37	48.6	5	60.0
20-24	23	43.5	12	33.3	10	50.0	1	100.0
25-29	15	40.0	5	20.0	6	50.0	4	50.0
Ethnicity								
Maori	32	31.3	19	26.3	11	36.4	2	50.0
Non-Maori	87	50.6	37	45.9	42	52.4	8	62.5
Residence (closest cancer centre)								
Auckland	51	37.2	26	26.9	22	40.9	3	100.0
Christchurch	17	58.8	9	66.7	7	57.1	1	0.0
Dunedin	8	100.0	3	100.0	5	100.0	0	-
Palmerston North	9	44.4	3	33.3	5	40.0	1	100.0
Waikato	20	35.0	10	40.0	7	28.6	3	33.3
Wellington	14	42.9	5	20.0	7	57.1	2	50.0
TOTAL	**119**	**45.4**	**56**	**39.3**	**53**	**49.1**	**10**	**60.0**

Diagnosis

65 deaths were recorded among the cohort, with follow up to 31 December 2013. No deaths of patients reviewed were attributed to causes other than their cancer. There appeared to be a slight improvement in AYA bone tumour survival in the latter half of the decade (survival for those diagnosed in 2005-2009 was 51.0% c.f. 41.4% in 2000-2004).

37 patients were recorded as having metastatic disease at diagnosis, 31% of those 118 patients who had their disease staging recorded. The proportion of metastatic osteosarcoma (23%) was comparable to what has been reported elsewhere. However, 40% of all Ewing tumours were metastatic, a much greater proportion than the 25% reported by SEER. For those patients who already had evidence of metastases at diagnosis, prognosis was grim; overall survival for the metastatic group was 13.5% compared to 59.3% for those with localised disease. The most common site of metastases was the lungs. Only 1 of 16 patients with lung metastases survived (6.3%) and of the seven patients with more than one metastatic site recorded, none survived.

	TOTAL BONE TUMOURS		TUMOUR GROUP					
			Ewing tumour		Osteosarcoma		Other bone tumour	
	n	observed survival (%)	n	observed survival (%)	n	observed survival (%)	n	observed survival (%)
Date of diagnosis								
2000-2004	70	41.4	36	33.3	29	44.8	5	80.0
2005-2009	49	51.0	20	50.0	24	54.2	5	40.0
Staging at diagnosis								
Localised	81	59.3	33	54.5	41	58.5	7	85.7
Metastatic	37	13.5	22	13.6	12	16.7	3	0.0
Not recorded	1	100.0	1	100.0	-	-	-	-
Diagnosis site								
Skull, face & jaw	6	66.7	-	-	5	60.0	1	100.0
Spine	3	66.7	3	66.7	-	-	-	-
Ribs	7	71.4	5	60.0	-	-	2	100.0
Chest wall	8	37.5	8	37.5	-	-	-	-
Upper limb	9	55.6	5	40.0	4	75.0	-	-
Pelvis	24	18.2	14	14.3	6	33.3	2	0.0
Lower limb	57	47.4	15	46.7	38	47.4	4	50.0
Other	7	57.1	6	50.0	-	-	1	100.0
Site(s) of metastases								
Non-metastatic disease	81	59.3	33	54.5	41	58.5	7	85.7
Bony	11	27.2	6	16.7	5	40.0	-	-
Lung	16	6.3	8	12.5	6	0.0	2	-
Multiple	7	0.0	5	0.0	1	0.0	1	0.0
Other	3	33.3	3	33.3	-	-	-	-
Not recorded	1	100.0	1	100.0	2	100.0	-	-
TOTAL	**119**	**45.4**	**56**	**39.3**	**53**	**49.1**	**10**	**60.0**

Symptoms at Presentation

An aspect of hospital presentation for bone tumours that has been thought to influence outcome is the time the individual takes to present. Therefore the subjective amount of time the individual had experienced symptoms expressed at their first hospital consultation was recorded. These patients presented to a tertiary care facility a median of 64 days after symptom onset (range: 0 days - 4 years). Compared with early presenters, late presenters in this study group showed no difference in disease progression at presentation. Localised and metastatic cases were evenly distributed between the two groups. However, those presenting under the median number of days had a survival rate of 37.5% while those patients presenting later than 64 days had a survival of 50.9%.

The most commonly reported symptoms at presentation were pain at the tumour site (n=29), a mass/lump (n=28), and swelling (n=14). Many of the symptoms at presentation were common, non-serious complaints that were not likely to have caused immediate concern to the patient or the clinician they first presented to.

Symptom(s) at presentation	Number reporting symptoms
Mass / lump	28
Pain at the tumour site	29
Pain in a nearby site	11
Breathing difficulties	3
Swelling	14
Pain from a prior injury	6
Fracture / injury	5
Other	9

Medical History

In terms of relevant medical history, three AYA diagnosed with osteosarcoma had a previous diagnosis which is associated with an increased risk of developing osteosarcoma in later life; one patient had NHL B lymphoma, osteogenesis imperfect, and Rothmund-Thomson Syndrome; one patient had Li Fraumeni Syndrome; and one had been diagnosed with bilateral retinoblastoma as a child for which they had received radiotherapy. In addition, one patient had been diagnosed with an enchondroma in the same site approximately eight years previously, and one patient had had a previous stress fracture caused by polyostotic fibrous dysplasia. For those diagnosed with Ewing tumours, relevant previous medical histories included septal defects (2 cases), chronic sarcroiliitis, osteomyelitis, and slipped upper femoral epeiphysis.

Referral Pathways

117 patients had their referral process documented in the available notes. Nearly every patient had their own unique referral pathway, highlighting the considerable complexities involved in treating this group of patients. The patient's residence, age, the centre in which they initially presented, their tumour characteristics and response all potentially influenced where they received their treatment. It is quite likely that there was, in some instances, greater consultation between different medical specialties/centres than was evident in the patient notes. In most cases it appears that the patients were seen in orthopaedics prior to referral to oncology services.

As would be expected, treatment centres documented in the patient notes were predominantly orthopaedics and adult oncology. In addition to the paediatric oncology service described above, other specialist services involved in the treatment of these AYA patients were respiratory (6), neurosurgery (7) cardio thoracic (3) and ENT (2).

Eight patients presented initially to the Emergency Department. Survival for these patients was 37.5% (3/8 patients) but there was no evidence to suggest that those presenting to ED were more likely to have metastatic disease (7/8 patients had localised disease). In addition, 3 presented to their physiotherapist, 4 presented to a private hospital, and 4 patients presented overseas.

Of the 4 patients presenting overseas, one was diagnosed in Australia and returned to New Zealand for treatment, and one had been diagnosed and treated in the United States but returned to New Zealand when they relapsed and their medical insurance ran out, and two patients came from Fiji for treatment. In all four cases these patients met the criteria for registration on the NZCR *but* their date of diagnosis was recorded as the date of histological diagnosis in New Zealand. Although the two Fijian patients were censored as alive as at 31st December 2013, it is possible that one or both patients subsequently passed away back in Fiji.

Treatment Centre

Of the 81 15-19 year olds diagnosed in this period, 29 were treated in paediatrics and 52 were treated within the adult service. 80% of all 15 year olds were treated in paediatrics, compared with 42% of 16 year olds and 12% of 17-19 year olds. During this time period 31 AYA aged 12-14 years were also treated exclusively in paediatrics.

Age at diagnosis	Treated in paediatrics	Treated in the adult service
(12-14 years)	(31)	-
15 years	16	4
16 years	8	11
17 years	1	11
18 years	3	11
19 years	1	15
TOTAL 15-19 years	**29**	**52**

Within the time period concerned, the vast majority of surgeries took place in either Christchurch, Middlemore, or Auckland. Therefore, a relatively large number of patients (56) were required to travel from outside of their usual residence to receive treatment at another centre. However, there was no clear evidence of survival disparities for those patients who were treated in more than one centre (46.4%) compared to those who were able to receive all their treatment in a single centre (44.4%).

Survival for 15-19 year olds treated in paediatrics was 51.7% compared to the adult service (44.2%). There was a greater difference in the observed survival for osteosarcoma (62.5% in paediatrics c.f. 38.1% in the adult service).

	TOTAL BONE TUMOURS		TUMOUR GROUP					
			Ewing tumour		Osteosarcoma		Other bone tumour	
	n	observed survival (%)	n	observed survival (%)	n	observed survival (%)	n	observed survival (%)
Service								
Paediatrics	29	51.7	11	36.4	16	62.5	2	50.0
Adult (15-19 years only)	52	44.2	28	46.4	21	38.1	3	66.7
Adult (Total)	90	43.3	45	40.0	37	43.2	8	62.5
Number of centres								
Single centre	63	44.4	33	36.4	22	50.0	8	62.5
Multi-centre	56	46.4	23	43.5	31	48.4	2	50.0
TOTAL	**119**	**45.4**	**56**	**39.3**	**53**	**49.1**	**10**	**60.0**

Treatment Protocol and Chemotherapy

As participation in clinical trials has been suggested in the literature as a factor influencing outcome, we collected detailed chemotherapy information.

A total of 15 bone sarcoma patients out of the 119 overall were enrolled in a clinical trial. Eight were treated in adult oncology (7 of whom were treated in Christchurch) and 7 were treated in paediatrics. Only two osteosarcoma patients were enrolled in a clinical trial and only around 30% of those with osteosarcoma were treated according to a named protocol.

Of the 56 patients diagnosed with a Ewing tumour during this period, half were treated according to a named protocol from an international study group, namely ANZCCSG (6), COG (6) or Euro-Ewings (15). 13 patients (23%) were enrolled in a clinical trial. Survival was higher for patients treated according to a named protocol (50%) compared to unnamed (31.0%) and for study patients (61.5%) compared to non-study patients (31.0%).

While 104 patients received curative chemotherapy, 35 did not complete their treatment as per the protocol. In 22 cases this was the decision of the physician (e.g. due to disease progression or chemo-toxicity) and in 9 cases it was the patient themselves who chose to not complete the treatment. The reasons were not documented for the remaining 4 patients. Contrary to expectation, there is no evidence to suggest that deviation from the protocol was associated with poorer survival.

Of those AYA with osteosarcoma who received chemotherapy, 45% were given methotrexate. Survival for those receiving methotrexate was 60.9% compared with 35.7% survival for those who didn't.

	TOTAL BONE TUMOURS		**TUMOUR GROUP**					
			Ewing tumour		**Osteosarcoma**		**Other bone tumour**	
	n	**observed survival (%)**	**n**	**observed survival (%)**	**n**	**observed survival (%)**	**n**	**observed survival (%)**
Enrolled in a clinical trial								
Yes	15	60.0	13	61.5	2	50.0	-	-
No	102	42.0	42	31.0	50	48.0	10	60.0
Not recorded	2	100.0	1	100.0	1	100.0	-	-
Named protocol								
ANZCCSG/COG/Euro Ewings	44	52.3	27	50.0	16	60.0	1	0.0
Unnamed/other	75	41.3	29	31.0	37	43.2	9	66.7
Chemotherapy completed according to protocol								
Yes	69	46.4	36	38.9	32	53.1	1	100.0
No	35	45.7	17	35.2	16	37.5	2	0.0
Not stated/no chemo given	15	66.7	3	66.7	5	60.0	7	71.4
Methotrexate								
Yes	-	-	-	-	23	60.9	-	-
No	-	-	-	-	28	35.7	-	-
Not stated/no chemo given	-	-	-	-	2	100.0	-	-
TOTAL	**119**	**45.4**	**56**	**39.3**	**53**	**49.1**	**10**	**60.0**

Surgery and Radiotherapy

31 different surgeons treated those 84 patients who had a surgical event recorded. Over half (44/84) of all surgeries were completed by one of three surgeons. These patients had a survival 61.4%, similar to the survival for those treated by other surgeons (57.5%). Survival for the 31 patients who did not have surgery recorded was only 6.5%.

72 out of 84 patients (86%) receiving surgery received it in one of the three specialist sarcoma surgical centres (Auckland, Middlemore and Christchurch). While survival for Middlemore was the lowest of the three, it is possible that Middlemore was referred the most complex cases and it must be remembered that surgery is only one component of the patient's treatment.

Radiotherapy was administered to 44 patients.

Pelvic Ewing sarcomas had particularly poor survival (14.3% for the 14 cases diagnosed in this period). In terms of staging, 6 were localised, 7 metastatic and 1 not recorded. In addition to chemotherapy, 3 of the 6 localised cases had surgery and radiotherapy, 1 had radiotherapy only, 1 had surgery only, and the other was not documented. All 7 metastatic cases had radiotherapy and 1 patient also had additional surgery.

	TOTAL BONE TUMOURS	
	n	**observed survival (%)**
Surgical centre		
Auckland	**26**	**61.5%**
Auckland	19	63.2%
Starship	7	57.1%
Middlemore	**28**	**39.3%**
Christchurch	**18**	**83.3%**
Other	**12**	**66.7%**
Dunedin	1	100.0%
Hutt	3	33.3%
Northshore	1	100.0%
P/N	2	100.0%
Private	1	100.0%
Waikato	4	50.0%
No Surgery	**31**	**6.5%**
Not Recorded	**4**	**50.0%**
Surgeon		
Surgeons with the highest number of surgeries*	44	61.4
All other surgeons	40	57.5
Grand Total	**119**	**45.4%**

*3 surgeons, each operating on at least 10 patients in the cohort

Disease Recurrence and Second Malignancies

59% of those diagnosed with Ewing tumours had disease recurrence. The median time that this occurred was 356 days from diagnosis (range: 26 days to 6 years). A similar pattern was seen for those with osteosarcoma; 52% had disease recurrence documented as occurring a median of 364 days from diagnosis (range: 56 days to 3 years 4 months).

In addition, one patient was diagnosed with Acute Myeloid Leukaemia three months after the recurrence of their Ewing tumour.

	TOTAL BONE TUMOURS		TUMOUR GROUP					
			Ewing tumour		Osteosarcoma		Other bone tumour	
	n	observed survival (%)	n	observed survival (%)	n	observed survival (%)	n	observed survival (%)
Disease recurrence								
Yes	60	6.7	32	3.1	26	11.5	2	0.0
No	54	87.0	22	90.1	24	87.5	8	75.0
Not recorded	5	60.0	2	50.0	3	66.6	-	-
TOTAL	**119**	**45.4**	**56**	**39.3**	**53**	**49.1**	**10**	**60.0**

Maori AYA

Maori AYA diagnosed with malignant bone tumours in 2000-2009 had particularly poor survival. A key aim of this retrospective chart review was to identify disease and treatment factors which could potentially account for this survival disparity.

Metastatic disease at presentation was very similar between NZ Maori (28.1%) and non-Maori patients (32.2%), as was the median time between symptom onset and presentation to tertiary care. The median time between symptom onset and presentation was 69 days for Maori (range: 10 days - 2 years 3 months) and 62 days for Non-Maori (range: 0 days - 4 years).

In terms of clinical trial enrolments, Maori were equally likely (or rather, unlikely!) as non-Maori to participate in a clinical trial, to be treated according to a named portocol, and to complete their chemotherapy as planned. There were some unique life situations in this Maori group which were documented as having impacted the treatment they received. One patient was in prison, one had drug taking and adherence issues, and one patient was pregnant and requested that her induction chemotherapy be delayed.

	ETHNICITY					
	Maori			**Non-Maori**		
	n	**%**	**observed survival (%)**	**n**	**%**	**observed survival (%)**
Stage at presentation						
Localised	22	68.8	40.9	59	67.8	66.1
Metastatic	9	28.1	0.0	28	32.2	17.9
Not recorded	1	3.1	100.0	-	-	-
Named protocol						
ANZCCSG/COG/Euro Ewings	11	33.3	36.4	33	38.0	57.6
Unnamed / Other	21	63.7	28.6	54	62.0	46.3
Participation in a clinical trial						
Yes	5	15.6	60.0	10	11.5	60.0
No	26	81.3	23.1	76	87.4	48.7
Not recorded	1	3.1	100.0	1	1.1	100.0
Completed chemotherapy according to protocol?						
Yes	19	59.4	21.0	50	57.5	56.0
No	9	28.1	44.4	26	29.9	30.8
Not recorded / no chemo given	4	12.5	50.0	11	12.6	72.7
TOTAL	**32**	**100**	**31.3**	**87**	**100**	**50.6**

Illustrative Case Summary

In October 2007 J.S., a 17 year old of Maori ethnicity, presented to Hutt ED seeking an ACC form. He stated that he had had a sore leg for 3 months, originally from a work injury, but recently the pain had become increasingly severe. His ankle was swollen and unable to weight bear. Following clinical investigations and biopsy, J.S. was diagnosed with non-metastatic osteosarcoma of the right distal tibia.

The initial treatment plan was for neo-adjuvant chemotherapy (2 cycles of high dose Methotrexate, Adriamycin, and Cisplatin) at Wellington Blood & Cancer Centre followed by limb salvage at Middlemore and 8 cycles of post-operative chemotherapy.

At the time of his diagnosis J.S. was living with his mother and siblings and also spent time at his girlfriend's house. In the first cycle of neo-adjuvant chemotherapy, it was noted that J.S. had issues with family instability and support around treatment. J.S. was not able to manage the Hickman line independently which often became infected and complicated the neo-adjuvant treatment.

A Hutt surgeon recorded in late February 2008 that J.S. had been receiving cycles of chemotherapy over the previous four months and that there had been delays between the bone tumour unit in Auckland and the Wellington oncology services over this period of time. An MRI indicated disease in J.S.'s ankle and limb saving surgery was no longer an option. Middlemore requested that a standard below knee amputation be performed at Hutt as soon as possible. This took place in early March and J.S. was discharged 3 days later.

Following J.S's discharge, the district nurses had considerable difficulties locating J.S. for follow up wound care at home. J.S. would come and go between houses and often changed his cell phone number or lost his phone. J.S.'s wound became infected and required further treatment. Concerns were recorded around J.S.'s use of cannabis with opiates.

In May 2008 J.S. was provided with an artificial limb. It was noted that he was finding the adjustment difficult. J.S. was on a benefit and living in a cold flat. He needed encouragement to take antibiotics and was becoming frustrated by the number of medications he was taking.

In August 2008, after completing 6 of the 8 cycles of post-operative treatment, J.S decided to stop chemotherapy. His oncologist noted that J.S.'s domestic life at this time was chaotic and that compliance was a huge issue for him. During the previous two cycles of treatment he had left the hospital against medical advice and did not present when he was febrile and a risk of neutropenic sepsis.

In April 2009 J.S's oncologist documented that when they last saw J.S. they were concerned by findings on his chest x-ray which raised the possibility of recurrent osteosarcoma but that J.S. did not keep his appointment for an urgent CT scan or attend a subsequent follow-up appointment. In June J.S. attended an appointment where he was told that the recent CT scan showed metastatic disease in his lung and abdominal lymph nodes and that this was now a palliative situation. J.S. passed away in March 2010.

Limitations

There are limitations to this study which should be considered. Firstly, four individuals have been involved in collecting the study data. In research projects such as this it is optimal, for consistency, to have one person responsible for retrieving and inputting the data in its entirety. Secondly, there are data gaps which could potentially have distorted the results and have prevented some analyses from taking place. For example, the chemotherapy treatment may have been described simply as 'VAC' without the recording of cumulative dosages. Or, the *intended* course of treatment was recorded, but it was noted elsewhere that this had been subsequently altered but not what it was altered to. Therefore it was not possible to examine if there was a relationship between chemotherapy dose intensity and survival. A final limitation is that quantitative data, no matter how comprehensive, cannot paint a complete picture of the unique experiences of each patient. Potential factors influencing patient survival outcomes such as social support available, health beliefs, and treatment adherence, are very difficult to quantify or to identify from patient medical records alone.

This study has highlighted considerable challenges for conducting AYA research at a national level. In general, there is a reluctance from the DHBs to allow researchers from other centres to access their patient records for research purposes. Although the study had HDEC approval, one DHB still refused to allow the researchers access to their patient records. Also, each DHB in New Zealand appears to have their own unique procedures for handling research requests which can result in lengthy waits and a considerable amount of active follow up required in order to obtain the necessary approvals. One DHB required the completion of their centre-specific application forms, Maori Research Committee sign off, and the appointment of a co-investigator employed at their DHB all before the request for *one patient file* could be added to the agenda for consideration at their next monthly Research Committee meeting.

It is recommend that if the AYA Cancer Network Aotearoa is undertaking any future research which involves chart reviews, they allocate additional funds for a research nurse to travel to each centre in order to retrieve the data. Any research project of this nature will also require several months lead-in in order to gain the necessary HDEC and locality approvals.

Discussion

65 AYA patients in this cohort died within the follow up period. It is worth highlighting that had the AYA survival rate been as it was for 10-14 year olds diagnosed with bone sarcomas during this same time period, 19 fewer deaths would have occurred. In fact, it is possible that the survival rate for this cohort was even less than the 45% reported, as two of the patients appear to have returned to Fiji and any overseas deaths would not have been recorded in our National Health Index.

This study found low numbers of AYA with bone sarcomas who were enrolled in a clinical trial, a well-known challenge for AYA oncology in general. Only 15 of the 119 patients in this cohort participated in an international collaborative clinical trial. Despite the small number of participants, survival was notably higher among those 13 Ewing sarcoma patients who were treated on study compared to those who weren't.

In terms of ethnicity, there are no apparent diagnostic or treatment differences evident in the data collected which could potentially explain the poor survival of Maori compared to non-Maori. It is possible that there are unique psychosocial issues among this group that are outside the scope of this chart review.

Finally, despite extensive efforts by those involved in the data collection, some data gaps still remain which have unfortunately prevented some planned analyses from being undertaken. We expected that it would be relatively straightforward to ascertain any deviations from the treatment protocol, cumulative dosages of chemotherapy and radiotherapy, and to identify *all* the centres where the patient received their treatment. The fact that it was so difficult to locate such information in the patient medical records provides evidence, in itself, that improvements could have been made in the case management that this cohort received. There was certainly suggestion in some patient records of gaps in communications between centres and subspecialties which may have resulted in suboptimal patient outcomes.

The sheer volume of data collected in this study, from resection margins, to referral processes, highlights the considerable complexities of treating this small subset of AYA bone sarcoma patients. Given the rarity of bone tumours, each centre (with the exception of Auckland) is likely to only see one or two AYA bone tumour cases each year. While this presents substantial challenges in terms of developing the requisite clinical expertise across all centres it also provides New Zealand with a unique opportunity to enact national changes in the treatment of this small group which will ultimately lead to improvements in their survival.

Despite the challenges which we faced in gaining access to patient medical records for this study, it is recommended that the AYA Cancer Network Aotearoa commences collecting prospective data for all AYA diagnosed with bone tumours in order to closely monitor this high-risk group. Given the small number of patients involved, the AYA Keyworkers may be in a position to collect patient data in their centres using a standardised template and report this back to the national group.