Morbidity of very long term (>30 years) survivors of allogeneic Stem Cell Transplant 1979-1989: a single centre experience

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INTRODUCTION

- The number of long-term survivors of haematopoietic cell transplant (HCT) is increasing worldwide
- Ten year survival of patients surviving disease free at two years post HCT was 85%[1] in a multi-centre study of >10000 patients (median follow up 9 years) but life expectancy remains below the general population.
- The cumulative incidence of a chronic health condition after HCT has been estimated as 59% at 10 years [2] but the burden of morbidity in patients surviving >15 years after HCT is less clear.
- In this study we have collected data on the morbidity of surviving patients who were transplanted 30-40 years ago.

METHODS

Data on morbidity were obtained from:

- Correspondence
- Electronic records

Data on survival and cause of death were obtained from:

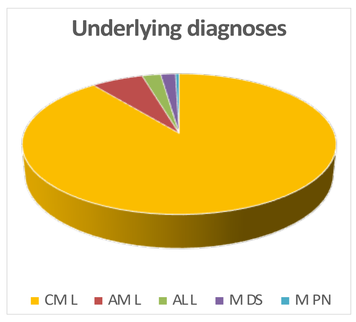
- Local online databases
- Death certificates
- The NHS portal

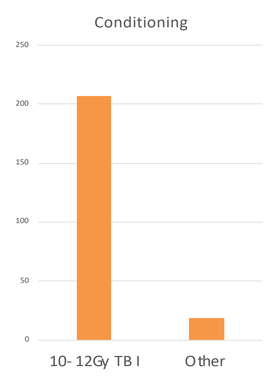
The NHS portal records patient death as an outcome if the patient is living in the UK when they die *and* they have an NHS number

RESULTS

226 patients were transplanted between 1979-1989

- **202/226 were transplanted for CML**





- **207/226 received 10-12Gy TBI**

Of 226 patients transplanted

- 164 /226 (72%) died
- 62 /226 (28%) were presumed survivors

Of 62 presumed survivors

- 15 are living abroad so no further information available
- 47 presumed in UK with no record of death on NHS portal
- **Data available for 26/47 (55%)**
- 18/47 lost to follow up (>4 years)
- 3/47 no data available

Characteristics of very long term survivors n=26	
Gender	Female n=13
Median age at HCT	27 years (range 14-42)
Median follow up time	33 years (range 30-40)
Median age at follow up	63 years (range 49-76)
Diagnosis	20/26 CML

TIMING AND CAUSES OF DEATH (n=164)

MORTALITY	0-100 days	100 days-2 years	2-10 years	10-20 years	20-30 years	30-40 years
N=	55/226	45/ 171	28/126	20/98	11/78	5/67
Relapse	2	18	12	5		
Graft failure	10	3	-	-		
GVHD	12	5	3	3		
pneumonitis	14	10	2	-	2	
infection	10	6	6	2	1	1
VOD	2	-	-	-		
MOF	2	-	-	1	1	
Other	3[a]	2[b]	2[c]	1[d]	-	-
Second malignancy		1[e]	1[e]	4[e]	3[e]	1[e]
Cardiac					1	1
Unknown			2	4	3	2

a. Cerebrovascular, cardiac failure, respiratory failure
b. Acute respiratory distress syndrome n=2
c. Suicide, brain haemorrhage
d. Pulmonary embolism
e. Second cancers were as follows: breast x 2, bladder x2, colorectal x 2, oesophagus, lymphoma, renal, stomach

With time after transplant (>10 years), relapse decreased as a cause of death and second malignancy increased

Morbidity was frequent in this group of 26 very long term survivors with a median number of chronic health conditions of 4 (range 1-9). The most common problems were acquisition of cardiovascular risk factors (dyslipidaemia, hypertension and diabetes), low bone mineral density, endocrinopathies (hypothyroid and low testosterone) and second cancers (non-melanoma skin cancer and second solid neoplasms)

Morbidity in long term survivors (n=26)	
Dyslipidaemia	N= 17
Hypertension	N=16
Diabetes	N=5
Overt ischaemic heart disease	N=5
Cerebrovascular disease	N=2
Reduced bone mineral density	N=13
Hypothyroid	N=12
Low testosterone	N= 3/13 males
Non-melanoma skin cancer	N=5
Second solid neoplasm	N=6
Chronic renal impairment	N=5
Chronic GVHD	N=5
Asthma	N=4
Gout	N=3
Irritable bowel syndrome	N=2

CONCLUSIONS

- Detailed follow up information relating to death or survivorship decreases with time after follow-up and this remains a challenge for transplant physicians.
- Amongst patients surviving > 20y, relapse and GVHD were notably absent as recorded causes of death; second cancers became more prevalent in patients surviving >10 y.
- In LT survivors, multi-morbidity was high with half of our survivors having four or more chronic health conditions.
- It is important that evolving strategies for following up this group of patients, take into account the clinical complexity of patients > 30 y after HCT.

REFERENCES

1. Wingard *et al.* 2011, JCO 29: 2230-2239
2. Majhail and Rizzo 2013, BMT 48:1145-1151.