The Prevalence Of Pain In Patients Attending Melanoma Outpatient Clinics

P Kuo, J Yen, A Gubbay, S Chapman, S Kandikattu, I Sohanpal, R Gupta, J Williams

Citation

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Abstract

Objectives: Despite literature reporting pain as one of the more common symptoms in patients with melanoma there are no accurate prevalence estimates for this population. Our aim was to therefore identify the baseline prevalence of pain in malignant melanoma, as well as its current management, so as to establish integrated pain pathways for our oncology colleagues. This information would also be considered in future research for the development of cancer specific pain pathways.Method: We recorded pain scores from those attending outpatient melanoma clinics in our tertiary cancer referral hospital. The characteristics of the pain and its management were assessed using the Brief Pain Inventory, the self-assessed Leeds Assessment of Neuropathic Symptoms and Signs pain scale and the Pain Management Index. We also investigated for associated risk factors (age, gender, tumor site, cancer treatment types) in presence and severity of pain. Results: 37% of patients investigated were in pain from any cause. 23% of patients with pain scored their pain as moderate to severe. 7% had a significant composite pain score of ≥5/10. 74% of patients with pain had a negative PMI signifying under-treatment. 59% had background pain for more than three months. Although the most common cause of pain was anti-cancer treatment, 43% had pain from non-cancer causes. 46% had neuropathic components to their pain however less than one third were prescribed adjuvant analgesics. We did not highlight any associated risk factors. Conclusions: Melanoma patients in the outpatient setting commonly experience pain which is chronic and undertreated. Many also have complicating neuropathic components which would benefit from specialist input. There were no associated predictors in the experience of pain. Approximately half of pain patients suffered from non-cancer sources. All patients attending melanoma outpatient clinics should be routinely assessed for pain to improve the overall quality of cancer pain management and these features are to be incorporated in future cancer specific pain pathways.

INTRODUCTION

Pain in cancer patients is often higher than expected and inadequately treated. A recent meta-analysis involving 52 studies documented prevalence as being approximately 53% [1] whilst a review using the Pain Management Index (PMI) – a recognized evaluation tool of analgesic strategy based on WHO guidelines [2] – demonstrated that 43% of cancer patients are undertreated with their pain [3]. This is despite repeated guidelines of treatment from international agencies [2,4,5,6] and bold statements proclaiming that over 90% of cancer-related pain should be manageable [5,7].

Various cancers display differing pain prevalence's [8]. Thus it is important to establish accurate figures for these groups and to determine the adequacy of treatment in order to raise awareness, provide detailed information on disease specific requirements and improve overall care. Whilst a majority of cancers have had published data on their prevalence, malignant melanoma does not.

The incidence of melanoma in the UK was estimated to be 11620 in 2008 [9] and in 2015 projections predict an incidence of 12400 [10]. In the WHO Europe region around 88500 new cases of melanoma occur each year [9]. The UK melanoma incidence rates for both men and women are above the European average having increased more than any other common cancer in the last 30 years [11]. With this increase is evidence of pain being one of the more commonly reported symptoms [12,13] although no reliable figures have been produced. The objective of this study was

to identify the prevalence of pain in malignant melanoma and to determine the effectiveness of its management so that correct and cancer specific treatment can be offered.

Cancer pain involves 'mechanisms of inflammation, compression and ischaemia causing varying degrees of nociceptive, neuropathic and visceral pains [14]' and the pathophysiology of malignant melanoma pain is no different. In particular, the neuropathic component has been adjudged to affect at least one-third of all assessed cancer patients [15,16]. Published risk factors for cancer pain are frustratingly confusing – age [17], gender [3,18], type of cancer [1,8], stage of cancer [19,20,21], presence of metastases [16,19,20,21,22], presence of breakthrough pain and decreased performance status [16] have all been indicated as predictors although none have been validated fully, especially with melanoma pain.

Patients with all stages of melanoma disease were surveyed whilst attending out-patient clinics at the Royal Marsden Hospital. Aetiology, duration and severity in pain were investigated as well as adequacy of pain control from evaluation of the PMI. Neuropathic pain and potential risk factors were also explored.

METHODS

The Ethics Committee of the Royal Marsden Hospital approved the study and it was registered with the Hospital Committee for Clinical Research. Good Clinical Practice Guidelines [23] and recommendations in the Declaration of Helsinki [24] were adhered to.

Patients attending melanoma outpatient clinics were approached between May to December 2009. The inclusion criteria were; patients aged 18 and above, a diagnosis of melanoma, an ability to understand and communicate effectively in English and the provision of informed consent to participation. Eligibility was extended to involve patients with advanced or metastatic disease and those receiving or having received anti-cancer treatments (surgery, chemotherapy, radiotherapy and/or biological therapy). Patients were only ineligible if their health would be compromised by participation in the study.

RECRUITMENT

All eligible patients were contacted via post or telephone the week prior to their appointment to inform them of the study. The research team (independent of the clinical team) approached these patients at their appointment to obtain informed consent. Patients recruited were then asked to complete a screening questionnaire with the assistance of the research team.

DATA COLLECTION

The following details were initially collected from the screening questionnaire:

Patient demographics: Age, gender, tumor site, treatment history (clarified with the electronic patient records)

Prevalence of pain: Pain in the previous seven days, analgesic medication taken.

Patients who had pain were then further assessed with regards to the characteristics and management of their pain.

Assessment of pain: Duration of background and breakthrough pains, aetiology (tumor pressure or infiltration, cancer treatment, or non-cancer related pain), pathophysiology (nociceptive, neuropathic or mixed), the Brief Pain Inventory (BPI) [25] and the self-assessment version of the Leeds Assessment of Neuropathic Symptoms and Signs pain scale (S-LANSS) [26] were all recorded. The BPI uses a collection of Visual Analogue Scales (VAS) to evaluate pain and its impact on daily function whilst the S-LANSS explores any neuropathic involvement using questions related to pain characteristics. Both are well validated tools of pain self-assessment.

Adequacy of pain management: The Pain Management Index (PMI) [3] was calculated for each patient. It is a simple index used to indicate a connection of the reported level of pain to the potency of the analgesics prescribed. The World Health Organization's 'analgesic ladder' [2] is used to grade the analgesics in question. A negative score suggests inadequate treatment.

Risk Factors: Determination of a relationship between pain and certain population sub-groups, location of tumour, disease staging or treatment types (i.e. surgery, radio-, chemotherapy or biological therapy) were all investigated. Binary logistic regression and ordinal regression were applied to identify these relationships. The analyses were performed using SPSS version 17.

OUTCOMES

The primary outcomes from this study were investigation of the prevalence of 'significant pain' and negative PMI in malignant melanoma. 'Significant pain' was given for scores of 5.0 or greater using a composite of the VAS for average pain, worst pain, least pain and current pain. Secondary

outcomes included duration, characteristics, pain prevalence and severity associated with the aforementioned risk factors and the proportion of patients with neuropathic pain as determined by S-LANSS.

POST STUDY SURVEILLANCE

Patients with pain, particularly those with a negative PMI, were offered further management in the following ways: assessment and management by the pain team, advice from the pain team together with contact details, advised to seek GP input or referral to an outpatient pain management clinic.

RESULTS

DEMOGRAPHICS

Patients were recruited from 27 melanoma outpatient clinics over the six month period; 12 surgical and 15 medical. From 140 eligible patients, 100 consented to take part. 40 did not participate due reasons outlined in Table 1. The age range of recruited patients was between 23 to 89 years, median 62 years. The gender ratio was 48% male and 52% female. Tumor sites are listed in Table 2. 59% had metastatic disease.

Figure 1

Table 1. Patients excluded from the study

Reason for exclusion	Number of patients excluded
Missed at clinic	22
Did not attend/cancelled	11
Refusal	4
Patient death/incomplete data	2
Histology unconfirmed	1
Total	**40**

Figure 2

Table 2. Tumour site and presence of pain

Tumour site	Pain in the last 7 days		Total	p-value
	Yes	No		
Arm	5	10	15	0.932
Leg	16	26	42	0.885
Trunk	12	18	30	0.632
Other	4	9	13	0.566
Total	**37**	**63**	**100**	

All p-values >0.05, hence all are non-significant

PAIN CHARACTERISTICS

In our study sample we found the overall prevalence of any pain in the previous seven days to be 37/100 (95% confidence interval 28– 47%). Using the range of 0-10 on the Visual Analogue Scale (VAS), 14/37 patients scored their pain as mild (VAS 1-4), 15/37 patients had moderate pain (VAS 5-7) and 8/37 (21%) patients admitted to severe pain (VAS 8-10). Therefore 23% of patients with pain scored their pain as moderate to severe. Significant pain (composite pain score of ≥5.0) occurred in 7% of the sample (95% confidence interval 2-12%).

PAIN DURATION

22/37 (59%) patients had suffered with background pain for over three months. Just under a third of patients had pain for more than one week but less than three months. Two patients had background pain for less than one week and a further two patients described no background pain at all.

BREAKTHROUGH PAIN

17/37 (46%) complained of problems with breakthrough pain for more than three months. Four patients had breakthrough pain for more than one week but less than three months. 16/37 (43%) had no breakthrough pain.

AETIOLOGY

18/37 (49%) patients felt that the pain was caused by their anti-cancer treatments. Of the remainder, 16/37 (43%) identified their pain to be unrelated to cancer (five musculoskeletal, four from unrelated surgery, three due to other conditions – osteoporosis, fibromyalgia and headache, four unspecified). Only three patients attributed their pain to direct tumor pressure or infiltration.

ADEQUACY OF PAIN CONTROL

Of the 37 patients with pain, 28 (74%) scored a negative PMI indicating inadequate treatment.

NEUROPATHIC PAIN

The research team analysed the subjects' pain characteristics for possible neuropathic components. Although 20/37 (54%) were assessed to be purely nociceptive, 15 patents (40%) elicited pain of mixed neuropathic and nociceptive origin and two (6%) stated pure neuropathic pain. Of these 17 patients with neuropathic involvement, only five were prescribed adjuvant analgesics such as anti-depressants or anti-convulsants.

Neuropathic pain was also considered from the S-LANSS questionnaire. 14/37 (38%) patients had scores of ≥12 and thus fitted the criteria. Three of these patients had significant pain (composite pain score ≥5) though none were severe

(≥8).

RISK FACTORS

Binary logistic regression used to analyse risk factors for the presence of any pain showed no statistical significance (Table 3): i.e. age (using 60 years as cut-off), gender, tumor site, cancer treatment types. Isolated limb perfusion as an anti-cancer treatment could be considered to be of marginal significance with a p-value of 0.07. Analysis with ordinal regression for those with pain showed no relationship between the severity of pain (i.e. mild/moderate/severe) and the risk factors shown in Table 4. Although the p-value in 'surgery for recurrence' is 0.03 this was felt unreliable due to the small numbers in some of the cells.

Figure 3

Table 3. Risk factors associated with presence of pain

Risk Factor	p-value
Age	0.839
Gender	0.753
Tumour site	All values >0.05 (see table 2 for details)
Radiotherapy	0.628
Isolated Limb Perfusion	0.071
Biological therapy	0.587
Chemotherapy	0.369
Anti-cancer surgery	0.999
- Surgery for recurrence	0.325
- Wide local excision	0.463

All p-values >0.05, hence all are non-significant

Figure 4

Table 4. Risk factors associated with severity of pain

Risk Factor	p-value
Age	0.783
Gender	0.453
Tumour site	All values >0.05
Duration of pain	All values >0.05
Radiotherapy	0.379
Isolated Limb Perfusion	0.309
Biological therapy	0.520
Chemotherapy	0.796
Anti-cancer surgery	
- Surgery for recurrence	0.035
- Wide local excision	0.176

P-values >0.05 are non-significant.

POST-STUDY SURVEILLANCE

Post-study surveillance was offered but not taken by all of the patients who complained of pain. 19/37 (51%) declined intervention. Of the remainder, nine were given advice and contact details for the hospital's pain team, two were advised to consult their GP for follow-up and two patients were referred back to their clinical teams for further investigation. Five patients were advised to contact their local pain services for further intervention.

DISCUSSION

In our study we found that the prevalence of pain in malignant melanoma patients attending outpatient clinics was 37%. This included all stages of disease. This figure is lower than the quoted figure of 53% in van den Beuken-van Everdingen's meta-analysis [1] despite two-thirds of our patients having metastatic disease. However as no previous prevalence scores have been documented this may reflect the baseline. More research is required to determine this.

With regards to our primary outcomes, i.e. 'significant pain' and negative PMI, 7% had a significant composite pain score of ≥5. Additionally, around a quarter of melanoma patients suffered from moderate to severe pain and over half of those with pain complained of chronic symptoms. Although these results were not analysed against stage of disease or phase of treatment, it demonstrates that these patients continue to suffer. Severe chronic pain in particular has been shown to increase mortality [27], whilst in metastatic malignant melanoma Coates et al. in 1993 indicated that pain was a significant predictor of subsequent survival (p = 0.004) [28].

However in other studies involving melanoma, overall quality of life, mood and appetite were shown to be more significant factors. More data is evidently required.

Remarkably 74% of our patients indicated a negative PMI and this is considerably higher than the 43% in Deandra's review of 26 studies [3]. Although this takes into account patients seeking help from alternative therapies such as acupuncture, massage or shiatsu it clearly indicates nearly three-quarters of our patients remain undertreated. Research demonstrates that inadequate treatment causes a multitude of morbidities ranging from the psychosocial; depression, anxiety [29,30] and poor personal interactions [31], to the physiological; poor sleep [32,33], neuroplasticity, chronic pain syndromes and immune suppression [23]. It can also lead to huge socioeconomic costs particularly in those of working age [8,30,34,35] with increased hospitalisations [36]. Pain has also been shown predict levels of 'utility' for cancer survivors of more than five years, 'utility' being a measure of the general health state by individuals and the general public. This association was significant for lung, breast and colon cancers, although in melanoma this was not proven to be statistically significant [37].

Asking patients to name the analgesics they took rather than those that they were prescribed provided a more accurate portrayal of their pain management plan. However it should be noted that the PMI is only an inference as to how pain is treated. It does not take into account complex issues of compliance, dose and route of administration, response to medication, use of adjuvant drugs and non-pharmacological therapies [3,38,39].

Anti-cancer treatment was the most common cause for melanoma pain corresponding with previous investigations in other cancer groups [40,41]. Clinicians are therefore reminded of this important complication which may be long-lasting if not adequately treated and it would seem prudent to include this information when consenting patients. The remainder mainly revealed their pain was not associated with the cancer. This re-emphasizes a holistic approach to care of the patient and the value of inter-disciplinary communications. Interestingly, only a small number of our subjects complained of pain related to the tumour. Several studies have previously found tumour-related pain to be the most common cause of cancer pain citing up to 90% [15,16]. Whether this is dependent on the cancer type could be the subject of further research.

As with other cancer groups [40,41], neuropathic pain featured highly. The assessment of the S-LANSS and descriptions of the pain characteristics demonstrated that between one third and half of our patients displayed criteria for significant neuropathic pain. This is higher than previous quoted values [15,16] and suggests a need to increase the use of adjuvant therapy to supplement conventional analgesics.

We were unable to identify any significant predictors in melanoma patients with the presence or severity of pain on statistical analysis. The risk factor with marginal statistical significance was found in patients who had undergone isolated limb perfusion reiterating the important consequence of anti-cancer treatment. The lack of predicting indicators may be due to insufficient sample size, pain from non-cancer causes or incorrect identification of possible risk factors. Notably however, doctors consistently rate pain as less severe than patients' own assessment, and this discrepancy is the strongest predictor of under-treatment of pain [42]. Anecdotally we found that routine screening for the prevalence of pain has resulted in an increased awareness amongst patients, oncologists and even pain specialists.

Finally, it is important to note that with over half of patients declining any form of surveillance from experienced pain clinicians, our ultimate goal of providing a service of screening for pain in outpatient clinics may require the need for a combination of screening and education of patients and staff to the benefits of pain management.

CONCLUSION

The prevalence of pain in melanoma patients at all stages of disease has now been identified. Whether this can be considered as the baseline requires further study. However we have shown that in a significant proportion pain is moderate to severe, has become chronic in duration and is largely undertreated. There were no obvious predictors as to who will experience pain and around half were caused by non cancer related aetiology. A considerable ratio had neuropathic involvement which can complicate treatment strategies and patients would benefit from specialist input. Clinicians are therefore reminded to routinely question patients in melanoma clinic as to whether pain is an issue so as to prevent a situation whereby the patient is suffering in silence with potentially adverse consequences.

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Author Information

Ping-Yi Kuo
The Royal Marsden Hospital NHS Foundation Trust

Jonathan TC Yen
The Royal Marsden Hospital NHS Foundation Trust

Anthony Gubbay
The Royal Marsden Hospital NHS Foundation Trust

Suzanne Chapman
The Royal Marsden Hospital NHS Foundation Trust

Subhash Kandikattu
The Royal Marsden Hospital NHS Foundation Trust

Imrat S Sohanpal
The Royal Marsden Hospital NHS Foundation Trust

Rajesh Gupta
The Royal Marsden Hospital NHS Foundation Trust

John E Williams
The Royal Marsden Hospital NHS Foundation Trust