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Chapter

Assessment and Management of Pain in Palliative Care

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Abstract

Palliative care is an essential component in any disease management. Pain assessment acts as the connecting link between the nerves, brain and spinal cord. Classification and assessment of the pain have great significance in controlling the pain-related symptoms. Pain is broadly divided into three types nociceptive, neuropathic and mixed depending upon the damage caused. Nociceptive pain is caused due to the stimulation of the pain receptors in the tissues and is further divided into visceral and somatic depending on the pain site. Neuropathic pain arises when the nervous system gets damaged or start dysfunctioning. Cancer pain assessment includes several factors like the site, intensity, syndrome, timing and temporal variation of pain. Edmonton staging system for cancer pain prognostic is widely used for pain management includes emotional/psychological distress cognitive impairment caused by pain. A comprehensive understanding of pain assessment will help in enhancing the quality of life of the patients.

Keywords: Pain assessment, Pain management, Nociceptive, Neuropathic, Opioids

1. Introduction

Pain is broadly defined as the unpleasant sensations in the body resulting due to the complex experience of various factors like physical, psychological and emotional [1]. Pain is subjective as pain tolerance differs from person to person. Pain cannot be quantified as it is associated with the effective as well as sensory components. Most cancer patients claim pain as the most common symptom and are quite dreaded, a major cause of anxiety [1]. Palliative care is an essential component in disease management. Good pain management is an important step towards palliative care. First of all, it is very important to understand the cause of pain, then assessment and manage pain, finally reassessment and monitoring the factors resulting in the pain. Managing and correct assessment of these symptoms are important for the wellbeing of the person to whom palliative care is being given.

It is very important to note that palliative care is intended to provide quality life by symptom control. To accomplish this, it is must to classify and assess the effects of pain. Pain is classified into various categories depending upon the duration, location, intensity and etiology of the pain (**Figure 1**). Pain can be acute or chronic depending on the duration of the pain. Acute pain is not long-lasting

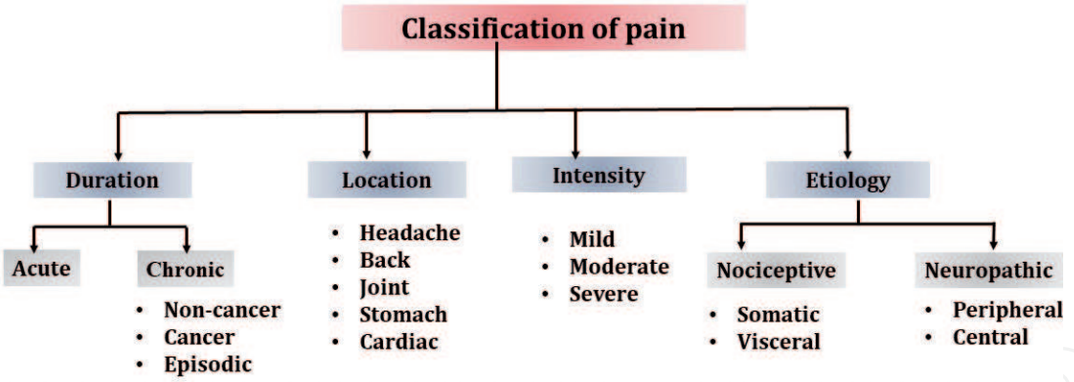

Figure 1.
Classification of pain.

as it gets resolved within a short duration whereas pain that cannot be resolved within six months is considered chronic pain. Chronic pain is further of three types: non-cancer, cancer and episodic. The intensity of pain ranges from mild to severe. Pathophysiology is mostly done by the utilization and knowledge of the damage caused to the tissue (nociceptive) and nerve (neuropathic) or could be unlocalized (visceral) or break-through that was given by the International Association for the Study of Pain (IASP) [2, 3]. It is noteworthy that pain can be physical as well as emotional. European Association for Palliative Care (EAPC) conducted an extensive review on the management of the use of pain assessment tools in palliative care research [3–5]. The newly revised version of cancer pain prognostics has included emotional/psychological distress, cognitive impairment caused by pain in the Edmonton staging system for cancer pain [4]. This improvement in pain prognostics has been able to be predictive than the previous methods used by IASP [3]. There are methods for the staging and progression of cancer like TNM Classification of Malignant Tumors (TNM). Unfortunately, there is no consensus on a single standardized tool for pain assessment [6]. The reason behind this is the varied nature of cancer and its malignancy and different perceptive and tolerance of pain in patients [6, 7]. Also, to blame is less predictability of the nature of tools available, as sometimes the mechanisms are not well known. To work on this problem, an extensive literature study on the physical, medical, psychological background and education on self-awareness/acceptance of pain should be deemed feasible.

2. Cause of pain

2.1 Nociceptive pain

It is also known as momentary pain. It is a form of acute pain caused by the triggering of nociceptive nerve receptors. This triggering occurs as a result of damaging chemicals or inflammation in the region [8]. A great example will be hitting your head on the table or stubbing your toe. Generally, nociceptive pain location is local. This type of pain gets notified by the nociceptors present throughout the skin and the internal organs. They can detect any chemical or physical damage send through the nervous system for immediate action [9]. There are two types of nociceptors as suggested by F. Cervero in 1985; one of them works for the fast transmission of pain called A-delta fibers whereas another one that slowly transmits pain is C–fibers [8]. The unmyelinated structure of C-fibres detects sudden pain while A-delta fibers detect pain arising due to noxious elements

or mechanical stress [8]. Increased abnormal sensitivity to the pain or chemical stimulus is named hyperalgesia caused by inflammation in the area [8–10].

Nociceptive pain is divided into two components:

- Somatic
- Visceral

2.1.1 Somatic pain

This type of pain arises from the stimulation of the nerve cells in the tissue such as skin, bones muscles, etc. due to damage [11]. Based on the site of cause the person can have superficial or surface-level deep somatic pain in bone or tendons and this type of pain comes in a flash as the injury is sustained [9, 11]. Due to the two varied nature of this pain person suffering from superficial pain will have an easier go at finding and pinpointing the pain rather than the deep somatic pain which is much harder to pinpoint as it diffuses easily and tends to radiate.

2.1.2 Visceral pain

Visceral pain occurs in cases when the person suffers from damage to the internal organs such as the intestine etc. The sensation of pain can be caused by damage to the tissue by external force or extensive pressure caused due to oncological reasons or infection in the abdominal organs [4, 8, 12]. This pain is not easy to pinpoint as the patient feels dull and as if squeezing most of the time due to the scarcity of the nociceptors [4]. Feeling in the area of damage detected by the nociceptors present in the abdominal cavity and on the organs it doesn't have a sharp onset visceral pain [8]. This effect is also termed as viscero-somatic convergence where the pain signal transported by afferent nerves converge with the nerves that are transferring pain from the say skin area can cause side effects such as nausea vomiting etc. [12].

2.2 Non-nociceptive pain

2.2.1 Neuropathic pain

This type of pain is characterized by the damage or improper function/misfiring of the neurons. The IASP defines neuropathic pain "pain initiated or caused by a primary lesion or dysfunction in the peripheral or central nervous system. A study by Martin, L. A., & Hagen, N. A. (1997) broadly classified them into peripheral and central neuropathic pain. Peripheral neuropathic pain has many sub iterations depending on the nerves involved. In a case study done by them, it was stated that out of 72 patients, six of whom had benign tumors, suffered central neuropathic pain [13]. This study concludes that the nerves that get damaged will start firing erratically with or without any nociceptive signal. Patients suffering from such chronic pain have reported that they experience pain constantly and are shooting in nature [13]. The pain can be triggered by a small number of stimuli or even without any stimuli. Multiple reports and studies suggest that hyperactivity of damaged neurons and further release of neurotransmitters, inducers, modulators, increase the effect [2, 10, 14]. Also, it is noted that the person's immune response to the pain releases cytokines which also elevate the neuropathic pain. Diseases such as diabetes, chronic back pain, alcohol consumption, cancer stroke are some reasons for this type of pain. The sympathetic nervous system can lead to the increased sensitivity

of the nerves. The release of hormones during flight/fight response increases awareness and due to this the nerves also get more sensitized leading to such pain suggested by Gierthmühlen, J. and R. Baron in 2016 [10].

2.2.2 Psychological effect on pain

Psychological factors are the major players in how the patient perceive the pain. Factors such as initial awareness, emotional status, interpretation and processing of pain and coping strategy play an important role in the perception of the pain [15]. Research on the effect of psychology and mental state by S.J. Linton and W.S. Shaw defines that initial detection of pain plays a crucial role in building up the psychological effects of it [16]. It is noted that pain needs attention and it is mostly under our conscious control. If the pain is deemed a threat, the autonomous nervous system kicks in, and also for later stages the object is likely to be avoided. Emotional state and interpretation can play a major role in sensitization and interpretation of pain [16]. Pain behaviour can be linked to how the person interprets the pain while suffering from it like verbal or non-verbal action and also after suffering from pain like the patient may start avoiding the source of stimuli as it generates the fear response. Negative thoughts about life such as anxiety, depression and fear can negatively affect the perception of pain and this may consequence in not only increasing the intensity but also prolonging the pain. Studies such as in S.J. Linton and W.S. Shaw in 2011 have shown 52% of people suffer from such a negative emotional state during pain [16]. Patients with imminent fear of the future also fall in this category and this all consequences in poor rehabilitation of the patient [15]. The next stage comes to coping with the pain, it has been seen that painful stimuli trigger the flight response with epinephrine released that can greatly affect the sensation of pain. [15, 16]. It can be inferred by this that in both cases, the sensation seems to be more tolerable as the person either avoids pain or confronts the source. The other method that seems to work is having a relaxed state of mind. Effects such as phantom limb pain are still considered to be a psychological phenomenon [17, 18]. Even though the limb does not exist, the pain is still perceived. In all, pain is greatly affected by the mental state of the person, but it has to be well understood and more studied.

3. Tools for analysing pain intensity

Pain intensity is subjective from person to person hence a common ground is picked which either in pictorial form or in the form of a questionnaire is communicated between the patient and the caregiver where the caregiver gets an idea of the situation and can plan before the treatment. These pain intensity tools play a major role in the assessment of pain and the tools used to analyze. There are many tools, but few are used quite often such as the McGill pain questionnaire, Wong-baker face pain scale, (**Figure 2**) visual analogue and numerical scales (**Figure 3**). Much of them work in a similar method by presenting the patient with a pictorial or a numerical based scale that the person can relate to and the person can pinpoint on which part of the scale he/she thinks the pain suffered stands [7].

3.1 Unidimensional pain assessment tools

The unidimensional assessment tool consists of mainly 2 categories which include the visual analogue scale or numerical rating scale and the pictorial rating

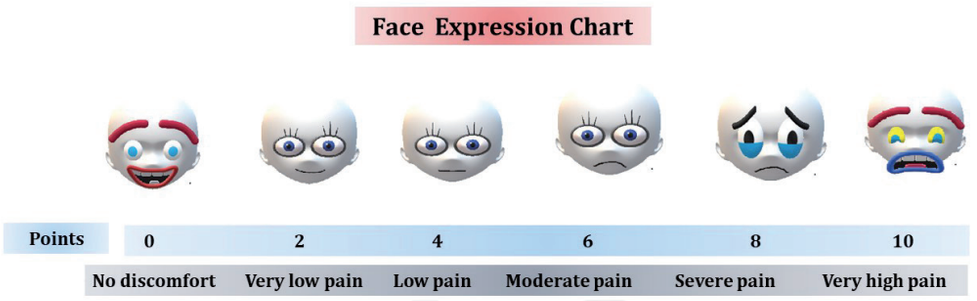

Figure 2.
Visual analogue pain intensity scale. Patient has to pin-point on where their pain stands on the scale [7].

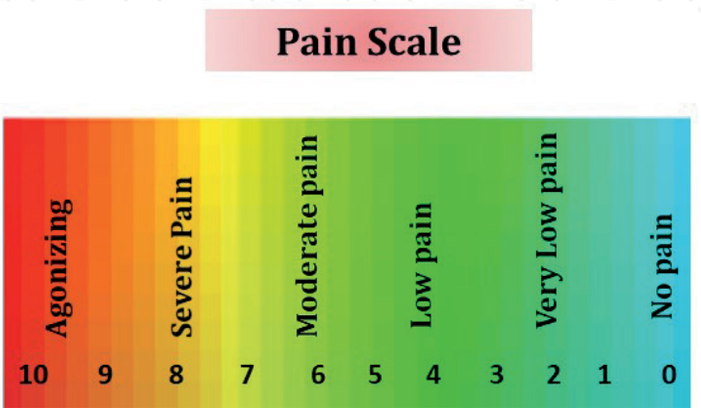

Figure 3.
Wong-baker face pain scale. The physician and the patient can look and state which expression they feel matches the scale. Ages 3 and above [7].

scale. These may or may not include verbal descriptions of the pain such as - moderate, severe, or less pain. In the visual analogue and the numerical method of scaling, a patient is asked to choose and mark the word or the number they compare/relate their pain to [17, 19]. The other method is utilizing the pictorial representation (**Figure 2**) such as faces which utilizes the comical representation of the reactions suffered during pain this method is best suited for children as it is difficult for them to translate a sensory experience to a spot on the scale example of such pictorial scale is Wong-baker face pain scale which utilizes 6 facial expressions describing the severity of pain [7].

The drawback of these methods is that these methods rely on the opinion of the patient and the opinion may vary due to different pain tolerance limits in different patients to the same pain sources [7]. Tolerance of a patient can be judged for a specific area using a dolorimeter which uses heat, electricity, or pressure to analyze the sample area's sensitivity and this can be later noted for further scaling [7].

3.2 Multi-dimensional pain assessment tools

As the name implies this type of tool assesses a patient on different levels/dimensions compared to the unidimensional pain assessment method. The Multi-dimensional method includes an assessment of more features such as the impact of pain, quality of pain and phenotype of pain for example to determine whether the person is suffering from neuropathic pain or not [19]. These tools utilize different types of the questionnaire to achieve its goal such as determining the impact and screening of the pain.

These include:

Brief Pain Inventory (BPI).
McGill Pain Questionnaire (MPQ).
Neuropathic Pain Scale (NPS).
Pain Quality Assessment Scale (PQAS).
Leeds Assessment of Neuropathic Symptoms and Signs (LANSS).
Neuropathic Pain Questionnaire (NPQ).
Douleur Neuropathique en 4 Questions (DN4) [20, 21].

3.2.1 Brief Pain Inventory (BPI)

BPI was developed by Collaborating Centre for Symptom Evaluation in Cancer Care, a team of WHO [22]. This is a method incorporated to assess self-reported pain severity and any interference in daily functioning, used in both clinical and research settings and is widely utilized and recognized in cancer pain assessment it is being self-administered and easy to access [7, 20, 23, 24]. It was approved and translated into many languages including Hindi, Spanish, Brazilian, etc. [22]. The subject is asked to fill up nine questions like if they have been feeling pain recently, location of the pain (a pictorial representation of both dorsal and ventral side of the human body which the subject can use to highlight the area of distress), pain intensity/severity during different intervals and other questions may include the effect of the drugs like an opioid taken for medication for pain management and lastly how pain affects your mood and your daily routine [25]. The scoring is divided into two categories that are pain severity and pain interference with a score of 0–10 where zero being no pain and ten being severe [25]. Similar scaling is done for interference also the final scoring is 0–40 and 0–70 respectively [25]. Multiple studies suggest that this two-dimensional tool (BPI) is quite adequate and is a capable method in analyzing pain intensity and pain interference caused due to neuropathic and nociceptive pain. In cancer pain assessment such as in a study conducted with 199 patients who underwent radiotherapy and results showed that there is a good correlation with an increase in pain intensity and its interference in the daily routine after radiotherapy [22].

3.2.2 Neuropathic Pain Scale (NPS)

As the name suggests it is a scale that is utilized for the differentiation in the neuropathic and non-neuropathic pain developed by Galer and Jensen [26, 27]. This scale contains 11 items for judging the qualitative and quantitative aspects of pain [20]. These items include pain intensity and its effect some items help in determining the features of the neuropathic pain such as sharpness, sensitivity, etc., and also how deep the pain is [28]. These items help in drawing a more accurate picture of the location and the quality of the pain widely utilized in the diagnosis of multiple sclerosis [20, 27, 28].

3.2.3 Pain Quality Assessment Scale (PQAS)

It is also a multidimensional scaling tool with questions that are explained descriptively such as sensitivity etc. In case of severity of pain, a numerical rating from 1 to 10 with ten being severe pain. The patient is advised to fill up/mark answers to the questions based on 20 items. These queries were recently revised by Mark P. Jensen in a cognitive revision test of the items to make them more understandable by the patients [21].

3.2.4 Leeds Assessment of Neuropathic Symptoms and Signs (LANSS)

LANSS was developed to address the less reliability of the NPS in neuropathic pain. This tool has a self-reportable version similar to BPI called S-LANASS with seven elements each weighted differently and is readily used in cancer pain assessment [20, 26, 27, 29]. Five questions mostly deal with yes or no questions for the severity, location, sensitivity, duration, etc. The last two questions are activity-based and require certain diagnostic actions such as gentle touching/rubbing the painful area [26, 29, 30]. These help in deducing if there is any nerve dysfunction, the final scoring is given by 24 [26, 29]. If the person receives a general score of less than 12 the pain is designated in the nociceptive section if the scoring is greater than 12 then the person falls in the category of neuropathic or Pain of Predominantly Neuropathic Origin (POPNO) [29, 30]. Originally designed by Michael Bennett has now been translated to many languages such as German Turkish, Chinese and even in Malayalam. It confirms the validation of this tool 101 chronic pain suffering patients were brought of which fifty patient were nociceptive and fifty-one were neuropathic the test concluded with a Cohen's Kappa 0.743(is a statistical analysis to test the reliability of a test with a range of −1 to +; generally >0.70 values are considered substantial) with 89.5% sensitivity [29, 31].

3.2.5 Neuropathic Pain Questionnaire (NPQ)

This is another method for judging and differentiating neuropathic pain from non-neuropathic pain [20]. A test regarding the validation on 528 chronic pain suffering patients of which 149 of them with neuropathic symptoms they were asked to fill up the NPQ with 12 items with the last 2 related effect of pain [32]. It was noted that it had a very low-reliability rate (66% sensitivity only) because of which it is not much popular as compared to the others [20, 30, 32]. Hence, it has been mainly used in the initial screening of neuropathic pain [20].

3.2.6 Douleur Neuropathique 4 Questions (DN4)

A ten-item scaling method utilized in the characterization of neuropathic pain has 4 questions that are simple to attempt with validated cognitive tests to prove its understandability to the patients it is administered to [21]. It has been translated into many languages and has a sensitivity of 83% [20].

3.2.7 McGill Pain Questionnaire (MPQ)

McGill pain questionnaire established by Dr. Melzack and Torgerson in 1971 at McGill University in Montreal, Canada is widely used in assessment tools for monitoring the intensity of pain [7]. Many studies have been conducted on the questionnaire such as by B Nicholson suggesting that it is a documentation method that utilizes the patient's experience like how he feels the pain, duration site, etc. [3, 7, 14]. A survey done by P. Kumar et al. showed that a total of 297 patients who underwent MPQ reported that it was qualitatively and quantitatively satisfying [7]. It gives multiple choices that help in identifying and in relating the pain suffered by the patient and these can be later compared with changes in a longer period of monitoring the patient [7, 14]. Not only that it also gives a human diagram to point out wherein the body the pain exists. With questions such as where your pain is? Is it internal or external? And the multiple-choice for how the pain changes with time, with this it seems to be quite regarded and efficient in diagnosing pain and related ailments [14].

4. Methods of pain assessment (pain assessment tools)

Assessment is the rigorous process of documentation, self-knowledge and interpretation. The need for cancer pain assessment during and after the treatment at the end-of-life stage is very important. Many contributing factors may affect the diagnosis of the source of the pain. Due to the varied nature complexity in the classification of pain, there is no consensus on a common pain assessment tool. This is to be noted and a common effective method should be there to evaluate the pain and its history in the patient. Since the pain assessed is in the boundary of cancer, the method to stage malignancy and its type is measured by TNM classification of cancer. Since its discovery, it has been proficiently helping in the further planning of treatment to be provided. With the staging ranging from 1 to 4 with the fourth being severe [3, 6]. TNM staging plays an important role in the assessment of the pain as it can convey information about size, if it is malignant or if it has spread into the lymph [6]. Similarly, widely used pain assessment tools are

- International Association for the Study of Pain -IASP assessment tool for chronic pain taxonomy
- Edmonton classification system for cancer pain -ECS-CP
- Cancer pain prognostic scale-CPPS [3].
- Alberta breakthrough pain assessment tool [33–36].

4.1 International Association for the Study of Pain (IASP)- Assessment Tool for Chronic Pain Taxonomy

It is a symptom sign-based type of deducing the effects of chronic pain in the patient. It is the list of diseases that provide information and classification of pain. Studies on the basis of the location of occurrence the pain, where it is present in the body. Next comes how the patient feels the pain like it is pinching, radiating or may be flickering in nature or does it change as time passes. This helps the clinical person to deduce the type of pain whether neuropathic or nociceptive and also possible organ system that is affected by the pain by deducing if it is visceral or somatic. The last consideration taken is the intensity of the pain [3, 14]. To extract this information, the patient is asked to fill up a questionnaire such as the McGill pain questionnaire which deals with [7, 14]. The problem with such classification of pain is that it is not predictive in similar aspects to TNM which is predictive and can give an idea on how to plan the treatment [3, 6]. Due to much-received criticism, changes were done in 2011 namely, the International Classification of Disease 11th revision (ICD -11) was for chronic pain groups such as chronic cancer pain involving the use of visceral and neuropathic pain and also adding continuous pain and episodic pain (pain that comes and goes) [2].

The IASP classification of chronic pain is done by using these following groups/ domains

Domain 1-The site where the pain occurs
Domain 2-Organ systems that get affected due to pain
Domain 3-Temporal characteristics deal with the frequency of pain
Domain 4-Intensity of the pain and time passed since its onset
Domain 5-Pain etiology [3].

4.2 Cancer pain prognostics scale

It is a numerical-based scale for characterizing and for running prognostic assessment of the condition and it is more predictive as compared to the previous ones. It is based on the scores ranging from 0 to 17, where the higher the scoring on this scale the good/better the prognosis and better chances of pain relief. Hence, this is a very useful tool in determining poor prognostics amongst patients [2]. This scaling has added features compared to IASP assessment for pain such as

Domain 1-Worst of pain
Domain 2- Emotional well-being of the patient
Domain 3- Pain characteristics
Domain 4- Daily opioid consumption [3].

Where scaling for worst pain is given from 1 to10, for emotional well-being is judged by using Functional Assessment of Cancer Therapy (FACT-G) and the daily opioid dose is monitored for greater than 60 mg consumption as its higher levels of it will make it difficult to control pain and person seems to be more tolerant [3].

4.3 Edmonton classification system for cancer pain (ECS-CP)

To improve on the IASP system of classification for chronic pain, there is a better versed and more widely accepted method of classification called ECS-CP (Edmonton Classification System for Cancer Pain) also is incorporated in the multisite of European Palliative Care Research Collaborative (EPCRC) [3, 4]. It is a more rigorous and user-friendly system of pain classification compared to the previous iterations for classifying pain. Additional descriptive features for pain classification are also incorporated such as the patient's emotional wellbeing. Other than this it incorporates seven components to evaluate the patient as suggested by Bruera E.[4]:

Domain 1-Mechanism of pain
Domain 2- Characteristics
Domain 3- Cognitive function
Domain 4- Previous opioid use
Domain 5-Psychological distress
Domain 6- Tolerance
Domain 7-History of such related pain [2, 4, 37].

Hence it is implied that this is better for further prognosis and pain treatment as this not only keeps check on the emotional/psychological distress but also considers the patient history of having difficulties in the same area or maybe similar types of pain [2, 4, 37]. Also, to be noted that it also checks whether if there is any case of taking opioids and if due to pain there is any cognitive impairment in the concerned patient though their involvement is still debated in the process of pain assessment in the newer version of this model. This method of assessment and prognosis of pain has widely been reviewed and validated in many studies and there is still improvement going on.

ECS-CP questionnaire categories are further dived into subcategories such as the understanding mechanism of pain it can be divided into the following subcategories (**Table 1**) [4]. These can be denoted by a letter such as N for the

S.No	Mechanism Of Pain (M)	Your Response	Characteristics Of Pain (C)	Your Response	Cognitive Function (F)	Your Response	Psychological Distress (P)	Your Response	Past History Of Addictive Abuse (A)	Your Response
1	Nociceptive Pain		Incident Pains		Normal Functioning		No Distress		Yes, Present	
2	Neuropathic Pain		Non- Incident Pains		Abnormal Functioning		Distress Present		Not Present	
3	No Pain Felt		No Incident Pains							
	Specify if, Psychological distress is present: _____ Specify if, Past history of addictive abuse: _____ *Result: M__C__F__P__A__*									

Table 1.
ECS-CP questionnaire.

category and subcategory can be in small caps alphabetic or numerical, the lower sub-feature as seen provides more information higher the chances of good prognosis. Similarly, for the rest of the groups depending on the new version such as opioid intake, tolerance, they are also divided into subcategories according to their function [2, 4].

4.4 Alberta breakthrough pain assessment tool (ABPAT)

ABPAT was developed by Alberta Cancer Board and the Alberta Cancer Foundation. It is an emerging tool for pain prognostics and works under the boundaries of assessing breakthrough pain. This method was developed by a knowledgeable panel of the reviewer by utilizing the Delphi process and conducting many patient's think-aloud interviews [34, 36] Breakthrough pain is generally categorized as a sudden increase or flaring of existing chronic pain such as in cases of cancer or joint-related problems [33]. It is reported that breakthrough pain in cancer patients, its occurrence is about 40–93%, hence quite common as it has come up quite a lot of times that no standardized assessment tool exists so the goal of Alberta breakthrough pain assessment tool was to provide a standardized format for research purposes [34]. Using the opinion of experts in this field reaching a consensus a questionnaire of 17 questions was put out. Next came the validation of this process, whether the patients were understanding what they have been asked to fill up so that the researcher added the think-aloud to judge the comprehensive and cognitive understanding of the people participating in the survey (**Figure 4**). This helped in the revaluation of their question by rigorous feedback from the participants and adding any changes in between.

The format of questions participants was asked:

- Relationship to the baseline pain
- Location and intensity of pain
- Quality, duration and frequency of pain
- Predictability of pain
- Response to medication [34].

This was well evaluated in a study conducted that was mentioned by Sperlinga R. where approximately 90% of the participants said that the questions were understandable and 80% said that it is a good tool for the breakthrough problem [35]. The validation and reviewing of the results were done both nationally and internationally such as in UK, Australia, Middle-East, Israel and North America and many respondents that participated in the survey were from medical nursing fields [34].

4.4.1 Why pain arises?

Pain is the 3rd most common symptom of cancer and reportedly has many reasons for the cause of pain from cancer [38]. It winds up being the patient-related factors such as, the location of the tumor, the neural system and the tissue being affected, stage of cancer its malignancy etc. People also suffer from pain related discomfort while going through the treatment of cancer which includes surgery for the removal of the tumor from the affected area, chemotherapy and radiotherapy

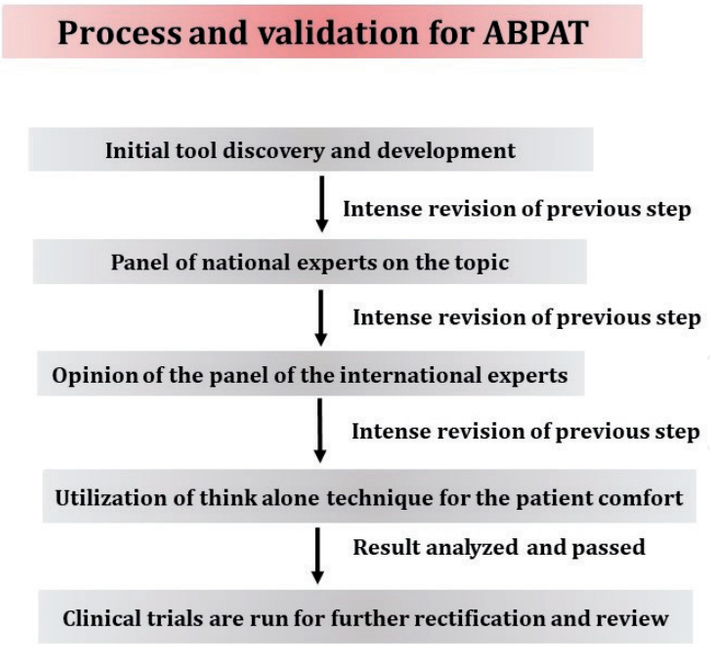

Figure 4.
Flowchart representing research design for ABPAT [34].

that the patient may be undergoing for managing cancer [39]. Hence cancer pain can be broadly divided into two categories

1. Pain caused due to tumor

2. Pain caused while undergoing treatment

Tumor related cancer pain mainly occurs due to excessive pressure on the nearby tissue or bone (Cancer-induced bone pain) and nerve causing the sensation of pain. Also, this can lead to blockages to a certain area and bodily mechanism of transport of nutrients, causing tissue damage which can cause both nociceptive pain and neuropathic pain if the nerves are damaged [38, 40]. Inflammatory responses can also be a major player in destroying affected areas such as in a study related to pancreatic cancer. It was noted that due to inflammation transient receptor potential cation channel gets activated which in turn activates Substance P (SP) and Calcitonin Gene-Related Peptide (CGRP) two neurotransmitters that transfer pain signals to dorsal root ganglia [38]. In the case of cancer-induced bone pain, cancer cells release RANKL (Receptor activator of nuclear factor kappa-B ligand) which increases the reabsorption of the bone by osteoclasts degrading the bone and sensitizing pain nerves [41, 42]. Drugs that are used in the treatment of neoplastic disease(chemotherapy) such as Bortezomib, Cisplatin, Vincristine, etc. although are widely used and effective but have a big downside of causing peripheral neuropathy by damaging sensory neurons, dorsal root ganglia and neurons present in the spinal cord [40]. Surgical procedures cause side effects in many cases and may have minor damage to the operated area. This can lead to neuralgia due to damaged nerve or in one study on myofascial pain syndrome caused after post breast cancer surgery. The neuromuscular damage after breast cancer surgery in the thoracic area stays contracted in pressure and is sensitive to myofascial trigger points [39, 43]. Even patients who are undergoing radiotherapy for head neck cancer have reported that radiotherapy results in other problems like mucositis in their buccal cavity and their throat and esophageal tract with severe lesioning [44]. These studies suggest that cancer pain can not only be caused by the tumor but also by the treatment that the person is undergoing.

4.4.2 Treatment and management

The best and widely accepted treatment in cancer pain is the utilization of opioids which are predominantly used for symptomatic treatment of pain [45]. Opioids function by binding to opioid binding receptors such as (mu, kappa, delta, and sigma) and these ligands and receptors are present throughout the body. Opioids function as inhibitory agents during excitation and in turn decreases the release of excitatory neurons [46]. Morphine is the most well-known among opioids [41]. These opioids such as buprenorphine, codeine, fentanyl, methadone, oxycodone, and tramadol are given in various methods such as oral, intravenous injection or drip, etc. The amount of dosage to be given is determined by the body-weight of the subject [46]. Various drugs have their benefits like fentanyl which can be used for rapid action in cases of oral administration it is also good for delivering transdermally including opioid buprenorphine [45]. Other methods include the administration of corticosteroids for anti-inflammatory effects. In the USA, this method is used against inflammation caused by cancer and related treatments in palliative care [47]. Similarly, the utilization of aspirin as a non-steroidal drug is also widely administered [47]. Recently due to much increase in cancer pain research, the analgesic abilities of marijuana (cannabinoids) are also being looked upon as a potential drug for pain mitigation. Another drug "oliceridine" which was recently approved in 2020 for cancer pain management in adults was found to have fewer side effects as it also activates G- coupled protein receptor based μ-opioid receptor and has therefore an analgesic effect with tolerance comparable to morphine [42, 48]. In cases where analgesic medicines are deemed ineffective, gabapentin or pregabalin are recommended for low dosage use.

Although opioids are well suited and effective against nullifying the effects of pain. Although, it has been well documented that if abused, they do have detrimental effects on the patient with higher doses having the possibility of addiction and then withdrawal from the drugs. Short-term effects still include nausea, vomiting, breathing difficulties and many more [46, 49]. This was validated by a study done by Kata V. on opioid abuse stating that in 2016 one of the top causes of accidental death in the U.S was opioid drug overdosing [49]. In the same study, it was also noted that due to breakthrough cancer pain requiring short-acting opioids and are required in frequent doses compared to long-acting opioids this can cause overdosing of the patient leading to complications [49]. A long-proposed idea is the use of non-opioids and non-steroidal anti-inflammatory drugs. In a study conducted by Janette Vardy and Meera Agar, they mentioned that multiple studies and research on more than 2000 patients were conducted and these patients were administered with acetaminophen [50]. It was noted that at various doses of acetaminophen ranging from 500–1000 mg, there was significant reduction in pain and there was no ill effect about the same. Furthermore, nonsteroidal anti-inflammatory drugs can become toxic in patients with cardiovascular and GI tract issues, indicating that even they have to be administered only after checking for these ailments on the patients [50]. For further research, proper mitigated administration of these pain repressing drugs should be followed.

5. Conclusion

Still, pain assessment remains quite challenging to the caregivers. The reasons being first there is no consensus available or a format that speaks a common language to the masses. Pain acts differently in individuals and even though two people suffer from the same ailments their pain tolerance will be affected by many

environmental and genetic factors. Differences in the site, the comprehension and pinpointing of the pain, the varied nature in intensity and the change in the same intensity due to previous/ongoing emotional turmoil, rendering the use of the same type of method for each obsolete. Many of the assessment tools are either disregarded or are still under heavy reviewing by peers. Some such as the IASP tool for assessment are unable to predict the future movement of pain symptoms and their debilitating effect. Though the ECS-CP, CPPS and ABPAT can predict to some extent they are not on par with the basic TNM staging of cancer. The intensity of the pain is very subjective and will vary from patient to patient.

The major problem of pain assessment is the subjective nature. The addition of emotional and psychological effects has been shown to produce more correlation between the subjective and the documented results and this will help in predicting the future pathway, the pain may take. Though this has been accomplished by the commonly accepted ECS-CP & CPPS but extensive review and research should be conducted such as in ABPAT with international validation (though it is still on-going). Also, assessment tools rather than being rigid can be multi-dimensional and include more domains specifically catering to the patient. This will not only provide a proper prognostic to the patient, but the caregiver will also be more prepared to administrate the required amount of analgesic /opioids to not only treat pain symptoms but also preventing any such overdosing of the drugs. And maybe increase the administration of drug alternatives that are not addictive such as non-opioids and nonsteroidal anti-inflammatory drugs. Hence, hopefully, this multi-dimensional pain assessment method might able to provide a smoother life during the patient's palliative care stage.

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Conflict of interest

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