Palliative Care Journal Watch

A partnership between Pallium Canada and several Divisions of Palliative Care and Medicine across Canada and Internationally:
McMaster University, University of Calgary, University of Alberta, Queens University, University of Toronto, McGill University, University of Manitoba, Hadassah-Hebrew University Medical Center

Project ECHO
Palliative Care - Canada
BY Pallium Canada

Hosts: Dr. Jose Pereira and Dr. Sharon Watanabe
Panelists: Dr. Aynharan Sinnarajah and Dr. Leonie Herx

Date: November 13th, 2024

Welcome to the Palliative Care Journal Watch!

- Keeps you up to date on the latest peer-reviewed palliative care literature.
- Led by palliative care experts from several divisions of palliative care/medicine across Canada and internationally.
  - McMaster University
  - Queen's University
  - McGill University
  - University of Toronto
  - University of Manitoba
  - University of Calgary
  - University of Alberta
  - Hadassah-Hebrew University Medical Center in Israel.
- We regularly monitor over 30 journals and highlight articles that challenge us to think differently about a topic or confirm our current practices.

The Palliative Care ECHO Project

The Palliative Care ECHO Project is a 5-year national initiative to cultivate communities of practice and establish continuous professional development among health care providers across Canada who care for patients with life-limiting illness.

The Palliative Care ECHO Project is supported by a financial contribution from Health Canada. The views expressed herein do not necessarily represent the views of Health Canada.

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What to expect from today's session

- We will present and discuss our featured selections and provide a list of honourable mentions.
- Please submit questions through the Q&A function.
- This session is being recorded and will be shared with registrants within the next week.
- This 1 credit-per-hour Group Learning program has been certified by the College of Family Physicians of Canada for up to **8 Mainpro+ credits** (each 1-hour session is worth 1 Mainpro+ credit).

Introductions

Hosts:

Dr. José Pereira, MBChB, CCFP(PC), MSc, FCFP, PhD
Professor, Faculty of Medicine, University of Navarra, Spain.
Clinical Professor, Division of Palliative Care, Department of Family Medicine, McMaster University, Hamilton, ON, Canada
Scientific Advisor and Co-Founder, Pallium Canada

Dr. Sharon Watanabe, MD, FRCPC
Director, Department of Symptom Control and Palliative Care
Cross Cancer Institute, Edmonton Zone, Alberta Health Services
Professor, Division of Palliative Care Medicine
Department of Oncology, Faculty of Medicine and Dentistry
University of Alberta

Panelists:

Dr. Aynharan Sinnarajah, MD CCFP(PC) MPH
Chair, Dr. Gillian Gilchrist Palliative Care Research, Division of Palliative Care, Queen's University and Lakeridge Health, ON, Canada

Dr. Leonie Herx, MD, PhD, CCFP(PC), FCFP
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Clinical Professor, Cumming School of Medicine, University of Calgary
Senior Scientific Director, Palliative Institute

Disclosures

Pallium Canada

- Not-for-profit.
- Funded by:
  - Health Canada (through contribution agreements 2001-2007, 2013-2018), Patrick Gillin Family Trust (2013-2016), Li Ka Shing Foundation (2019 to current), CMA (2019 to 2022), Boehringer Ingelheim (dissemination of LEAP Lung courses 2019 to current).
  - Partnerships with some provincial bodies.
  - Revenues from LEAP course registration fees and licenses, sales of Pallium Palliative Pocketbook.

This ECHO program has received financial support from:

- Health Canada in the form of a contribution program.

Disclosures of Hosts/Guest Panelists:

- Dr. José Pereira: Scientific Advisor, Pallium Canada.
- Dr. Leonie Herx: No conflicts of interest to declare.
- Dr. Sharon Watanabe: No conflicts of interest to declare.
- Dr. Aynharan Sinnarajah: No conflicts of interest to declare.

Mitigating Potential Biases:

- The scientific planning committee had complete independent control over the development of course content.

Featured articles

- Chang TW, Yang FY, Liu YC, Hung CH. **Gabapentinoids for chemotherapy-induced peripheral neuropathy: systematic review and meta-analysis**. BMJ Support Palliat Care. 2024 Aug 19;14(3):269-278. doi: 10.1136/spcare-2023-00436 https://pubmed.ncbi.nlm.nih.gov/38936970/
- Silva GAD, Oliveira LC, Wiegert EVM, Calixto-Lima L, Cunha GDC, Peres WAF. **Prognostic risk stratification using C-reactive protein, albumin, and associated inflammatory biomarkers in patients with advanced cancer in palliative care**. Curr Probl Cancer. 2024 Aug;51:101115. doi: 10.1016/j.currproblcancer.2024.101115. Epub 2024 Jun 28. PMID: 38943779. https://pubmed.ncbi.nlm.nih.gov/38943779/
- Bischoff KE, Patel K, Boscardin WJ, O'Riordan DL, Pantilat SZ, Smith AK. **Prognoses Associated With Palliative Performance Scale Scores in Modern Palliative Care Practice**. JAMA Netw Open. 2024 Jul 1;7(7):e2420472. doi: 10.1001/jamanetworkopen.2024.20472. PMID: 38976269; PMCID: PMC11231792. https://pubmed.ncbi.nlm.nih.gov/38976269/
- Meehan CP, White E, CVitan A, Jiang L, Wu WC, Wice M, Stafford J, Rudolph JL. **Factors Associated With Early Palliative Care Among Patients With Heart Failure**. J Palliat Med. 2024 Aug;27(8):1001-1008. doi: 10.1089/jpm.2023.0539. Epub 2024 Apr 12. PMID: 38608234. https://pubmed.ncbi.nlm.nih.gov/38608234/

Gabapentinoids for chemotherapy-induced peripheral neuropathy: systematic review and meta-analysis

Article Reference:
Chang TW, Yang FY, Liu YC, Hung CH. Gabapentinoids for chemotherapy-induced peripheral neuropathy: systematic review and meta-analysis. BMJ Support Palliat Care. 2024 Aug 19;14(3):269-278. doi: 10.1136/spcare-2023-00436

Selected by: Leonie Herx

Presented by: Leonie Herx

Summary of Key Points:

- Chemotherapy-induced peripheral neuropathy (CIPN) is a common side effect of chemotherapy with a prevalence of 30-55%
- CIPN impacts quality of life & may interrupt treatment thereby impacting its effectiveness
- Gabapentinoids are commonly used for the treatment or prevention of CIPN but evidence is inconsistent on their effectiveness for both treatment & prevention
- There is currently no comprehensive systematic review/meta-analysis on the safety & efficacy of gabapentinoids in CIPN

Methods used:

- Search of PubMed, Cochrane, Embase & ClinicalTrials.gov from inception to Sept 2022
- Terms: ‘chemotherapy’, ‘peripheral neuropathy’, ‘chemotherapy-induced peripheral neuropathy’ AND ‘gabapentin’ OR ‘pregabalin’
- Eligibility criteria:
    - RCTs evaluating efficacy/safety of gabapentin (GB) or pregabalin (PG) for treatment or prevention of CIPN
    - Adults 18yrs & older with cancer
- Statistical analysis: meta-analysis with RevMan V.5.4 & Metafor package in R
- Quality of RCTs evaluated with Cochrane Risk of Bias tool
- Primary outcomes: average pain & worst pain, quality of life (QOL), National Cancer Institute Common Terminology Criteria for Adverse Events (CTCAE)

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Selected by: Leonie Herx

Presented by: Leonie Herx

Key Results/Findings:

- 2344 publications identified, 8 met inclusion criteria
- 631 patients included in analysis (428 F, 203 M), avg age 50-55 yrs, variety of cancers.
- Chemotherapies mixed: oxaplatin-based, taxane-based & doxorubicin
- 4 studies for prevention & 4 for treatment of CINP

1. Safety of gabapentinoids (meta-analysis outcome)

– meta-analysis of 4 trials comparing gabapentinoids to placebo, risk of dropping out due to A/Es and fatigue not statistically significant compared to placebo. GBs had similar effect as placebo on: dizziness, N/V, diarrhea and rash.

2. Prevention of CIPN

PG vs Placebo (meta-analysis outcome)

- 2 trials: colorectal cancer, oxaliplatin & paclitaxel
- no significant improvement in average pain, QOL or grade 3+ A/Es vs placebo.
- Trend towards decreasing worst pain but not statistically significant.

GB vs Placebo (descriptive outcome)

- 2 trials – i) Breast ca and paclitaxel: more gd 2 & 3 toxicities in placebo, GB group had no Gd 3 neuropathy; ii) Head &neck ca: less pain at 7weeks than placebo

Summary results for prevention: PG does not significantly improve average pain or QOL in preventing CIPN than placebo. Unable to summarize for GB.

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Treatment of CIPN – descriptive outcomes

GB vs Placebo

- 1 study: adults with colorectal ca and CIPN >1 month – crossover design, 2x 6-week phases with 2-week washout.
- No benefit over placebo.

PG vs GB

- 1 study, PG vs GB for 8 weeks (various cancers, paclitaxel/paclitaxel & carboplatin).
- Both groups showed reduction in pain at 8 weeks.

PG vs duloxetine

- 2 studies for taxane-induced NP in breast cancer, paclitaxel or docetaxal.
- No differences in pain, QOL and neuropathy score.
- Duloxetine had higher insomnia but improved emotional functioning.

Summary results for treatment: no meta-analysis possible, no consistency in studies and no definitive benefits over placebo.

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Selected by: Leonie Herx

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Discussion:

- Heterogeneity of sparse data and inconsistent findings.
- For safety – overall safe
- For prevention of CIPN:
  - gabapentinoids do not significantly reduce the incidence or severity of CIPN
  - evidence too weak to warrant their use without further study.
- For treatment of CIPN:
  - some studies have shown a potential therapeutic effect but results inconsistent, lacking definitive benefits over placebo.
- Overall message:
  - No clear data to support the use of gabapentinoids in CIPN
  - More comprehensive and higher quality research is needed

Strengths:

- First systematic review & meta-analysis for safety and effectiveness of gabapentinoids in CIPN
- Included 8 RCTs with 631 patients

Limitations:

- Small number of included studies
- Insufficient sample size to allow for subgroup analysis
- Inclusion of different types of cancer & treatments increases uncertainty in results

Discussion

Prognostic risk stratification using C-reactive protein, albumin, and associated inflammatory biomarkers in patients with advanced cancer in palliative care

Article Reference:

Da Silva G, Oliveira LC, Wiegert EVM, et al. Prognostic risk stratification using C-reactive protein, albumin, and associated inflammatory biomarkers in patients with advanced cancer in palliative care. Curr Probl Cancer. 2024 Aug;51:101115. doi: 10.1016/j.currproblcancer.2024.101115.

Selected by:

Jose Pereira

Presented by:

Jose Pereira

Background

- Accurate prediction of survival helps decision-making and care planning in cancer care.
- Different prognostic tools available for patients with cancer, but suboptimal accuracy.
- Use of inflammatory markers and indices derived from them proposed:
  - C-reactive protein (CRP) and albumin serum levels
  - modified Glasgow Prognostic Score (mGPS) and the CRP/albumin ratio (CAR)
- Different prognosticating thresholds have been proposed but often dichotomous
  - e.g., CRP ≥10 mg/L; albumin <3.5 g/dL) (oversimplified?)

Study Aim/Objective

- To evaluate the prognostic value of CRP, albumin, CAR, and mGPS at different thresholds in patients with advanced cancer in palliative care.

Study design

- Prospective cohort study; pts on PCU in Brazil between July 2016 and March 2020.
- Inclusion criteria: pts ≥ 20 years old, Karnofsky Performance Status ≥ 30 %.
- Exclusion criteria: Absence of laboratory data and previous diagnosis of autoimmune and infectious diseases.
- Different thresholds analyzed:
  - CRP < 5 vs. 5-10 vs. > 10 mg/L, albumin < 2.4 vs. 2.4-2.9 vs. 3.0-3.5 vs. > 3.5 g/dL; CAR <1.2 vs. 1.2–2.0 vs. > 2.0, and mGPS equal to 0 vs. 1 vs. 2.
- Evaluated predictive accuracy of these thresholds to predict death within 90 days.

Prognostic risk stratification using C-reactive protein, albumin, and associated inflammatory biomarkers in patients with advanced cancer in palliative care

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Selected by:

Jose Pereira

Presented by:

Jose Pereira

Results

- 1,877 pts included (of 2153 original cohort).
- Patient characteristics
    - Median age: 62 (IQR 53-71). Females 57%
    - Different cancers (GI, gyne, H&N most common)
    - KPS: median 50% (40-60)
    - Median overall survival: 51 days (19-124)
    - 64% of pts died within 90 days
- Median survival (OS) 7.5x times lower in pts with albumin <2.4g/dL than >3.5
- Median survival (OS) 4x times lower in pts highest CRP, CAR and mGPS
- Survival curves: Significant differences in 90-day OS found across three thresholds for CRP, albumin, CAR and mGPS (p<.001)
- All markers and indices able to predict 90-day mortality i(multivariate model)
- CAR
    - ≥ 2 associated with highest risk of 90-day mortality than other markers
    - Showed best predictive accuracy (C-statistic 0.80)

Limitations

- Single center and did not exclude pts with acute infections; not studied by cancer type

Why is this article important?

- Inflammatory markers and their severity can be used to predict prognosis in pall care.
- CAR thresholds provide best discriminatory power.

Discussion

Prognoses Associated With Palliative Performance Scale Scores in Modern Palliative Care Practice

Article Reference:

Bischoff KE, Patel K, Boscardin WJ, O'Riordan DL, Pantilat SZ, Smith AK. Prognoses Associated With Palliative Performance Scale Scores in Modern Palliative Care Practice. JAMA Netw Open. 2024 Jul 1;7(7):e2420472. doi: 10.1001/jamanetworkopen.2024.20472. PMID: 38976269; PMCID: PMC11231792.

Selected by: Aynharan Sinnarajah

Presented by: Aynharan Sinnarajah

Summary of key points:

- Palliative Performance Scale (PPS) often used as a prognostic tool
- Developed in Victoria (1990s): Home-based and Inpatient PCU
- Limitations of existing research on prognoses associated with PPS scores
- Current prognostic estimates are based on outdated data, primarily from hospice or inpatient settings with short prognoses
- Majority of outpatient studies have focused only on cancer patients

Methods used:

- University of California, San Francisco
- Prognostic study design using electronic health record data linked with Vital Records
- Patients who received palliative care consultations: Jan 1, 2018 - Dec 31, 2020
- Demographic data (e.g. sex, race/ethnicity)
- Examined association between PPS scores and 1-month, 6-month, and 12-month mortality
    - Cancer vs Non-cancer
    - Outpatient: In-person vs Video telemedicine
- Bivariate analyses, Kaplan-Meier curves, and parametric survival analyses, adjusting for age, gender, and diagnosis group

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Selected by: Aynharan Sinnarajah

Presented by: Aynharan Sinnarajah

Key Results/Findings:

- N=4779 patients (47.6% inpt; 64.4% outpt); 63.5 yrs average age; 51.0% female.
- By 30 months (end of f/u), 61.2% inpts and 43.7% outpts had died.
- Mortality highest within 1st month after PPS
- If survived to 12 months, all groups were low and similar
- Prognoses associated with PPS scores were substantially longer (2.3-to 11.7-fold) than previous estimates commonly used by clinicians
- PPS had good ability to discriminate between patients who lived and those who died in the inpatient setting
- PPS had lower discriminative ability in the outpatient setting
- Mortality rates were higher for patients with cancer than other serious illnesses at most PPS levels, particularly in the outpatient setting
- No difference in in-person vs video telemedicine in outpt

Discussion:

- Inherent uncertainty in prognostication
- Short-term estimation (1 month) is ok especially inpatient
- Outpatient: Don't just rely on PPS
- Seems like video telemedicine can reliably be used for PPS calculation
- Updated ePrognosis calculator (https://eprognosis.ucsf.edu/calculators/) with their findings to provide clinicians with more accurate prognostic estimates based on modern palliative care data
- Future research is needed to examine PPS trajectory and compare the PPS to disease-specific prognostic tools in the outpatient setting

Prognoses Associated With Palliative Performance Scale Scores in Modern Palliative Care Practice

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Selected by: Aynharan Sinnarajah

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Additional Comments:

- Interesting to think about why, these prognoses have improved
  - Better disease treatments
  - Earlier palliative care
- What about type of cancer and sub-type even, and type of non-cancer illness?
  - Likely variations within those. E.g. new lung cancer treatments means their prognosis likely now longer
- How does this compare to Canada?
- Is it useful to also measure patterns in local jurisdiction?

Strengths:

- It was conducted at a single health system, although the inpatient and outpatient palliative care practices were large and the patient population came from across the state

Limitations:

- The study population was younger and less racially diverse than typical palliative care populations
- There were not enough patients with multiple PPS measurements over time to examine whether PPS trajectory is associated with prognosis
- The study was limited to 30 months of follow-up
- There were not enough patients with multiple PPS measurements over time to examine PPS trajectory, or to separate diagnoses into more specific groups beyond cancer vs. non-cancer.
- Also, only patients who saw palliative care. Unclear if applies to wider cohort.

Discussion

Factors Associated With Early Palliative Care Among Patients With Heart Failure.

Article Reference:

Meehan CP, White E, CVitan , et al. Factors Associated With Early Palliative Care Among Patients With Heart Failure. J Palliat Med. 2024 Aug;27(8):1001-1008. doi: 10.1089/jpm.2023.0539. Epub 2024 Apr 12. PMID: 38608234.

Selected by:

Jose Pereira

Presented by:

Jose Pereira

Background

- Heart failure (HF) is prevalent life-limiting condition associated with high burden of symptoms and needs.
- Increasingly calls to integrate palliative care (PC) in HF management
  - Evidence of benefits to patients, families and health care system
- Pts often not referred for [palliative care] and when they are, usually late in the illness

Study Aim/Objective

- To explore patient factors associated with receiving PC in HF

Study design

- Retrospective cohort study (secondary analysis) of U.S. Veterans with prior hospitalization to Veterans Affairs (VA) hospitals who died from 2011 to 2020.
- Categorized pts according to:
  - “Received PC” or “Not Received PC”
  - For “Received”: “Late” (PC < 90 days before death); “Early” (PC ≥ 90 days before death)
- Identified as receiving PC by “stop codes” in database (PC team)
- PC services across all VA hospitals

Factors Associated With Early Palliative Care Among Patients With Heart Failure.

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Selected by:

Jose Pereira

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Results

- n=232,079 Veterans
  - Mean age 76.5 ± 10.7 years
  - Males: 98% male
  - Comorbidities: Dementia (38%), cardiac dysrhythmias (67%), valvular disease (26%), chronic lung diseases (57%), renal disease (52%), depression (34%), malignancy (28%)
- No PC before death: 56.5% (*n* = 131,122)
- PC < 90 days before death: 22.5% (*n* = 52,114)
- PC > 90 days before death: 21.0% (*n* = 48,843)
- Veterans who died without PC tended to be younger with fewer comorbidities.

Discussion and author conclusions

- Many HF patients never receive PC, and many very late
- PC involvement seemed to be driven by comorbidities rather than HF.
- Effective collaboration with Cardiology is needed to identify patients who would benefit from earlier PC involvement.

Factors Associated With Early Palliative Care Among Patients With Heart Failure.

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Selected by:

Jose Pereira

Presented by:

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Limitations

- Predominance of males; Did not exclude possibility of PC provided by others; Did not study quality of PC or composition of PC teams in different VA centres.

Why is this article important?

- Highlights opportunities for improvement in integrating palliative care in HF management.
- What article does not do: Discuss role of generalist palliative care provided by cardiologists and cardiology teams

Discussion

Honourable Mentions

- Painter JT, Peng C, Burlette M, Clement C, Luciani L, Azhar G, Dayer L. **The Effect of Concurrent Use of Opioids and Gabapentin on Fall Risk in Older Adults**. J Pain Palliat Care Pharmacother. 2024 Jun 10:1-7. doi: 10.1080/15360288.2024.2358953. Epub ahead of print. PMID: 38857121. https://pubmed.ncbi.nlm.nih.gov/38857121/
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Wrap-up

- Please fill out our feedback survey a link has been shared in the chat!
- A recording of this webinar and a copy of the slides will be e-mailed to registrants within the next week.
- To listen to this session and previous sessions, check out the Palliative Care Journal Watch podcast.

Listen on Apple Podcasts

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NOTE: recordings, slides and links to articles from all our sessions are available at www.echopalliative.com/palliative-care-journal-watch/.

Thank You to our Journal Watch Contributors!

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