

ABSTRACTS OF KAUFMAN PAPER PRESENTATIONS

THE CONTINUING UNDER-TREATMENT OF OLDER MEN WITH LOCALIZED PROSTATE CANCER

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Background: There is significant uncertainty in clinical practice as to optimal treatment for patients with localized prostate cancer. Our primary goal was to analyze patient and disease specific factors that led to sub-optimal treatment for patients with localized prostate cancer.

Methods: A cohort of patients with localized prostate cancer diagnosed in 1995-1996 was used to compare the predicted life expectancy (LE) and quality-adjusted life expectancy (QALE) for each patient's actual treatment versus optimal treatment based on our previously described Markov state transition model. Differences in predicted LE and QALE between the actual and optimal treatments of ≥ 0.2 years were considered sub-optimal treatment.

Results: 41 of 276 patients (14.9%) received sub-optimal treatment based on QALE results. 39 of these 41 patients (95%) were under-treated with watchful waiting. Age, tumour grade, and co-morbidity were all significant predictors of sub-optimal treatment. Healthy men aged 70-79 with moderately or poorly differentiated tumours had the highest percentage of sub-optimal treatments (17 of 28 men, 60.7%). The average LE and QALE losses for this group of men was 0.98 y and 0.68 y per patient, respectively.

Conclusion: Otherwise healthy men in their 70s and 80s with localized prostate cancer are generally receiving watchful waiting and potentially losing valuable years of life. Many of these patients with at least moderate grade disease may benefit from curative therapy (radical prostatectomy or radiation therapy) but are not receiving it.

ALLEVIATING BREATHLESSNESS: A CRITICAL APPRAISAL OF THE LITERATURE ON THE MANAGEMENT OF DYS-PNEA IN PALLIATIVE CARE

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Background: This systematic review examines the evidence for the management of dyspnea in palliative care, a common and distressing symptom. Strategies available to primary care physicians were evaluated.

Methods: Medline was searched from 1966 to 2002 using "dyspnea", "breathlessness" and "palliative care" to determine management strategies. Secondly, searches were conducted by combining "dyspnea", "breathlessness" and MeSH headings for individual management strategies. Key texts and review articles were also examined for management strategies and references. Original research, including randomized clinical trials and lesser levels of evidence (open trials, case series, chart reviews) were reviewed. Studies that described strategies available to primary care physicians were included, (i.e. not surgery, chemotherapy, or radiation therapy) provided that they could be applied to a palliative population, and that dyspnea was a formally measured outcome.

Results: 64 studies were appraised. Non-pharmacological methods such as relaxation, acupuncture and acupressure, chest wall vibration, and a fan directed on the face appear to reduce dyspnea. The evidence is unclear regarding oxygen therapy, but it may benefit both hypoxic and non-hypoxic patients. Benzodiazepines have not been shown to be effective for dysp-

nea. The evidence for buspirone is conflicting. Chlorpromazine may reduce dyspnea. Opioids reduce dyspnea, both in enteral and parenteral routes. Nebulized opioids do not reduce dyspnea.

Conclusions: Physicians have many options in the management of dyspnea. Non-pharmacological strategies should be encouraged if available, especially the use of a fan. A trial of oxygen may be warranted in hypoxic and non-hypoxic patients. If anxiety or agitation is associated with dyspnea, buspirone or chlorpromazine may be reasonable options. Opioids are clearly beneficial in oral, rectal and parenteral routes. Nebulized opioids and benzodiazepines are not effective. Further research is needed to compare agents and to clarify optimal routes and doses.

USE OF ANTICHOLINERGIC MEDICATIONS BY INDIVIDUALS WITH DEMENTIA

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Background: Use of medications with anticholinergic effects (ACEs) has been associated with the development and severity of delirium, other types of cognitive dysfunction, and impaired self-care skills. Dementia may predispose individuals to these adverse ACEs. There is the potential for pharmacological antagonism when drugs with ACEs and cholinesterase inhibitors (ChEIs) are used concomitantly.

Methods: The primary objective of this study was to look at the prevalence of the use of medications with significant ACEs in participants of the second cycle (1996-97) of the Canadian Study of Health and Aging. These participants were categorized as NCL (no cognitive loss), CIND (cognitive impairment no dementia), and demented. Three listing of drugs with significant ACEs were used - Tune (J Clin Psychiatry 2001, 62<Suppl 21>:11-14), Saskatchewan Health (SH), and Roe (J Am Geriatr Soc 2002, 50:836-42). While there was little overlap between Tune and SH (6/49) or Roe (4/49), about half of the drugs were common between SH and Roe.

Results: Among participants with dementia, 57.6% were taking at least one agent on the list developed by Tune. The equivalent figures for SH was 32.7% and for Roe was 29.1%. For the use of two or medications on the lists the figures were 28.7%, 5.1%, and 4.0% respectively. For the SH and the Roe listings, use of an agent with ACEs was more common in those with dementia compared to participants categorized as CIND or NCL ($p < 0.001$) and among those on more medications ($p < 0.001$). Use was associated with lower Modified Mini-Mental State scores among CIND subjects (SH, $p = 0.003$; Roe, $p = 0.01$) and worse function in those categorized as NCL or demented ($p < 0.02$).

Conclusion: Use of agents with ACEs was common, particularly among participants suffering from a dementia. In this cross-sectional study use was associated with worse cognition and function.

PATTERNS OF BENZODIAZEPINE USE AND RISK OF INJURIES IN THE ELDERLY

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Background: Due to concerns about the increased risks of falls, as well as physiological dependence, benzodiazepines have come under intense scrutiny and criticism. Previous studies on the risks of injuries from falls associated with benzodiazepine use have methodological limitations that might affect the accuracy.

cy and precision of results and contribute to the inconsistency of the findings. The objective of this study was to evaluate the risk of injuries from falls associated with aspects of patterns of use, such as duration of users and cumulative dose, for individual products in an elderly population.

Methods: In a cohort of 78,367 new elderly benzodiazepine users, time-dependent covariates, representing past duration of benzodiazepine use and past cumulative dose, incorporating weighting by recentness of use, were calculated. Four Cox proportional hazards models with different time-dependent covariates were used to estimate the impact of individual benzodiazepine use on risk of injuries from falls. T0 was set to the date of the first prescription and all analyses were adjusted for baseline patient characteristics. Negative log likelihoods were compared to determine goodness-of-fit.

Results: All benzodiazepines except clonazepam were significantly associated with an increased risk of injuries from falls ($p < 0.05$). The best predictive model for triazolam, oxazepam, alprazolam, bromazepam, temazepam and clonazepam included cumulative duration and current dose. The best models for lorazepam, nitrazepam, chlorthalidopoxide, diazepam and flurazepam included cumulative dose. The optimal weight function varied among benzodiazepines.

Conclusions: Benzodiazepines were associated with an increased risk of injuries from falls in elderly patients, however duration of exposure may be more critical than current dose. Physiological dependence and withdrawal symptoms appeared to play an important role in increasing the risk for many benzodiazepines.

A PROSPECTIVE STUDY OF DETERMINANTS AND CLINICAL CORRELATES OF DECLINING DHEAS LEVELS IN OLDER MEN AND WOMEN: THE RANCHO BERNARDO STUDY

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Background: Dehydroepiandrosterone sulphate (DHEAS) levels decline with age, but most studies have been cross-sectional. The predictors and clinical correlates of change are poorly defined.

Methods: DHEAS was measured at baseline in 2219 community-dwelling men and women aged 30-77 (mean age 62) in Rancho Bernardo, California. DHEAS assays were repeated in the same laboratory 12 years after study entry in 416 men and 246 postmenopausal women not taking hormone replacement therapy or corticosteroids. Anthropometric data, lifestyle habits, medication history, comorbidities (cardiovascular disease, cancer, arthritis, diabetes, emphysema, depression) and subjective measurements of physical and emotional function were ascertained at baseline and at follow-up. Annual percent changes in DHEAS levels from baseline were calculated across age and sex strata. Multiple linear regression models were used to identify determinants and clinical correlates of DHEAS change.

Results: DHEAS levels were higher for men than women in every age group at baseline (mean values 1794 + 1045 ng/ml vs. 771 + 533 ng/ml respectively, $p < .0001$), with annual declines more pronounced in men (-4.0% vs. -2.2%, $p < 0.0001$). Baseline DHEAS levels accounted for 80% of the variability in DHEAS change over time in a model adjusted for sex and BMI at baseline. Smoking and weight change were not significant predictors of change ($p > 0.05$). The magnitude of DHEAS change was not associated with disease, functional status, or any other health indicators at follow-up.

Conclusion: Decreasing levels of DHEAS appear to reflect an

aging phenomenon, with no relationship between declining DHEAS levels and negative health outcomes.

WHAT CHARACTERIZES THE IDEAL GERIATRIC DAY HOSPITAL (GDH) PATIENT? A 6-MONTH RETROSPECTIVE CHART AUDIT AND PROSPECTIVE SURVEY OF GDH REFERRALS

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Background: Referrals to Geriatric Day Hospitals (GDHs) come from a variety of sources, including geriatricians, community family physicians, emergency room physicians, in-patient hospital wards, home care personnel and other professionals. The majority of referrals to GDHs are appropriate, as evidenced by improved outcomes. However, a proportion of patients referred to GDHs from various sources are sub-standard candidates for such programmes and result in misuse of valuable professional time and resources.

Methods: In the present study, a retrospective chart audit was conducted of all attendees to a local GDH during a 6-month period ($n = 126$). Data were collected on patient demographics, referral sources, reasons for referral, pre- and post-GDH goal attainment, pre- and post-GDH measures of disability and responses from a formal caregiver survey. Data were analyzed in order to assess patient outcomes and agreement between referral reasons, patient goals derived by the GDH assessment team and a caregiver survey.

Results: The mean goal attainment score (GAS) was 47.4 (SD=8.1), very close to the theoretically expected values of mean 50 and SD 10, indicating that most patients had realistic goals. Only 18 of 89 total attendees with completed goals had a GAS < 40, indicating sub-optimal outcomes. The goal areas with the most significant beneficial change in goal attainment were mobility, balance, falls, pain, emotional, socialization, medications, incontinence and caregiver stress (range of mean change in goal areas 0.7-1). In addition, GDH team personnel were surveyed, in a subsequent six-month prospective analysis, regarding personal opinions about patient suitability before and after attending the GDH programme. There was general agreement between team members' subjective responses and the results of the chart audit.

Conclusion: The present study shows that suitable GDH candidates with a good probability of success may be chosen prior to GDH attendance.

SHORT- AND LONG-TERM OUTCOME AFTER INTRAVENOUS RECOMBINANT TISSUE PLASMINOGEN ACTIVATOR (IV-RT-PA) FOR ACUTE STROKE IN PATIENTS 80 YEARS OF AGE OR OLDER

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Background: IV-rt-PA for acute stroke is standard of care. NINDS trial showed the effectiveness of this treatment in patients under age 80. A retrospective study found comparably favorable outcome between patients under age 80 or above at the time of discharge.

Methods: Prospective follow-up. Consecutive patients, 80 years or older, who received IV-rt-PA for acute stroke. Outcome measures: temporally cumulated numbers of survival, disability, death, cause of death, NIH-stroke-scale-score (NIHSS-Score), Barthel-index-score (BI), modified-Rankin-score (mR). Enrolment period: 23-months.

Results: Among 83 consecutive patients who received IV-rt-PA, 22 were 80 years of age or older. Admission NIHSS and cumulative outcomes are summarized in the table. Four deaths were from acute or recurrent strokes, 5 from sepsis, 2 from car-

diac causes.

Outcome at follow-up	Admission NIHSS Score Mean (range)	Cumulative Number of patients & (%)
Total number patients		
age 80 or older	15 (6-22)	22 (100%)
Died:	18 (11-22)	
In hospital		6 (27%)
by 3 months		6 (27%)
by 12 months		10 (45%)
by >12 but <24 months		11 (50%)
*Dependent	13 (9-19)	
at 3 months		8 (36%)
by 12 months		8 (36%)
at > 12 months		9 (41%)
Independent living	9 (6-14)	
at 3 months		3 (14%)
at 12 months		3 (14%)
at >12 months		2 (9%)

*mean Barthel-score: 30 (range 0-85); mean modified-Rankin-score: 4 (range 3-5)

Conclusion: The great majority of elderly patients who received IV-rt-PA for acute stroke did poorly in short and long term follow-up. More studies are needed to assess the effectiveness of IV-rt-PA for acute stroke in this patient population.

SEMME'S WEINSTEIN MONOFILAMENT TEST IN THE ELDERLY

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Background: The Semmes Weinstein monofilament (SWM) is widely used in the diabetic population. The older, non-diabetic population is also at risk for falls and foot ulcers, and the SWM could be a useful test.

Objectives: 1) To determine the reliability of the SWM in seniors. 2) To compare the SWM to vibration sense and ankle jerk. 3) To determine the percentage of seniors with abnormal SWM tests. Population: Convenience sample of 75 persons >70 years of age with no self-reported diabetes, from a geriatric day hospital, inpatient unit, and from the community.

Methods: Responses to the 5.07/10 g monofilament, vibration sense with the 128 Hz tuning fork, ankle jerk, and foot strength were measured. LEAP "Diabetic Risk Scores" were calculated. Inter-rater reliability was determined on a sub-sample of 19 participants.

Results: The "Diabetic Risk Score" demonstrated acceptable inter-rater reliability (Spearman's 0.62, $p < 0.001$). The SWM also demonstrated acceptable inter-rater reliability for the number of sites with lost sensation per foot (0-4), Spearman's correlation coefficient was 0.52 ($p < 0.001$). Ankle jerks and vibration sense at the MTP also demonstrated good inter-rater reliability. There is poor correlation between the SWM and ankle jerks, and poor correlation between the SWM and vibration sense. Impaired protective sensation was common, with 29% having an abnormal "Diabetic Risk Score".

Conclusion: The SWM is reliable in the elderly. Further research is needed to determine if sensory measures such as SWM or vibration sense predict falls or foot ulcers.

OPTIMAL INITIAL THERAPY FOR STABLE MULTI-VESSEL CORONARY ARTERY DISEASE IN THE ELDERLY: A DECISION ANALYSIS

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Background: Coronary artery disease (CAD) is a major cause of morbidity and mortality in the elderly. There is debate over the relative merits of different forms of therapy for CAD in older

patients. Although revascularization procedures have benefits over medical therapy in terms of efficacy, there are trade-offs including the risk of peri-procedural complications. Recently, several studies have suggested that even well-selected octogenarians can derive significant benefits from the use of revascularization strategies. Study Question: What is the best initial management strategy for older patients with stable multivessel CAD: coronary artery bypass grafting (CABG), percutaneous transluminal coronary angioplasty (PTCA), or medical therapy?

Methods: We constructed a decision analysis model using Markov processes to examine the optimal initial management strategy in 75-year-old men with stable multivessel CAD: CABG, PTCA, or medical therapy. Measurements: The primary outcome was quality-adjusted life-years (QALYs).

Results: The base-case analysis revealed that medical therapy was associated with 9.435 QALYs, CABG was associated with 9.394 QALYs, and PTCA with 9.162 QALYs. In testing our assumed probabilities and utilities in the sensitivity analyses, PTCA was found consistently to be the least preferred strategy across a wide range of values.

Conclusions: This model suggests a toss-up between medical therapy and CABG as the preferred initial strategy for chronic stable angina in the elderly. The model also suggests that PTCA is consistently the least preferred of the three management strategies.

THE EFFECTS OF ENDURANCE AND STRENGTH TRAINING ON MEASURES OF HEART RATE VARIABILITY IN HEALTHY ELDERLY FEMALE SUBJECTS

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Background: Prior investigations in post-myocardial infarction and healthy elderly subjects have established that heart rate variability (HRV) predicts mortality. Predominantly cross-sectional studies have shown an association between endurance training and measures of HRV. In a randomized trial, this study sought to prospectively compare the effects of endurance and strength training on HRV in 40 healthy elderly females (average age 69.9±0.9 years).

Methods: All subjects were rigorously screened to be normal by history, physical, blood tests, ECG, ETT and echocardiogram. All subjects were monitored for 24 hours by a 2-channel Holter before and after training. Artifacts and arrhythmias were manually removed. Tapes were examined for mean heart rate (HR), standard deviation (SDNN), standard deviation of 5-minute mean RR-intervals (SDANN), mean of all 5-minute standard deviations of RR-intervals (SD), root-mean square of difference of successive RR intervals (rMSSD) and the proportion of adjacent RR-intervals more than 50 msec different (pNN50). A Fast Fourier Transform was performed on all data to obtain total power (TP). 3 subjects were excluded due to excessive PAC's or low lead voltages. Intervention: 9 subjects were randomized to endurance trained (ET), 14 subjects to strength training (ST), and 14 subjects to no training (NT) for six months.

Results: The increase in VO₂max in the ET (+4%, $p = 0.01$) and the ST group (+4%, $p = 0.05$) was significantly higher than in the untrained group. There was a small but not significant decrease in HR with both the ET and ST groups. ET resulted in a significant increase in all measures of HRV, except for RMSSD and SD. ST resulted in no significant change in HRV measures.

Conclusion: Strength training, as opposed to endurance training has no significant impact on HRV. This suggests that exercise interventions designed to improve strength (such as weight-lifting) will have little to no impact on cardiovascular risk.