SERTIFIKAT

Ucapan terima kasih diberikan kepada

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Atas partisipasinya sebagai

PEMBICARA

pada Webminar Pokdi-Neurogeriatri dengan topik

"***Safety Consideration on the Pharmacological Treatment of Chronic Pain in the Elderly***"

Jakarta, 18 Oktober 2018

Dr. dr. Yuda Turana, Sp.S
Dekan FKIK Unika Atma Jaya/Ketua Pokdi Neurogeriatri

FKIK Unika Atma Jaya-Pokdi Neurogeriatri

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- Pain Management, Mumbai, India, 2012
- Diabetic Neuropathy Workshop, , Manila, Philippine, 2012
- USG for Neurologist, Jakarta, 2012
- Neuropathic pain workshop, Milan, Italy 2012
- USG Guidance for Interventional Pain management, Bandung 2012
- Pain Management Camp, Singapore 2013
- Interventional Pain Management, Medan 2013
- USG Guidance In Pain management, Yogyakarta 2014
- Asia Facific Pain Summit, Denpasar 2016
- Neuropathic Pain, Yokohama, Jepang 2016
- Dry Needling, Perth, Australia, 2017

Safety Consideration on the Pharmacological Treatment of Chronic Pain in the Elderly

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Denpasar-Bali

Outline

- Common Chronic Pain Problems in Elderly
- Factors to be considered
  - Physiological Change
  - Comorbidities
  - Drug Related Complications
- Recommendation

Common chronic geriatrics pain syndromes

- Rheumatic disease (ostheoarthritis, rheumatoid arthritis)
- Cancer pain
- Angina
- Postherpetic neuralgia
- Temporal arteritis
- Atherosclerotic and diabetic peripheral neuropathic pain
- Trigeminal neuralgia
- Malnutrition
- Peripheral vascular diseases
- Ischemic pain

Complexity of the elderly in pain management

- Physiologic change
- Cognitive change
- Comorbid condition
- Caregiver's knowledge
- Lack of evidence-based practice, training, awareness, and thorough understanding from clinicians

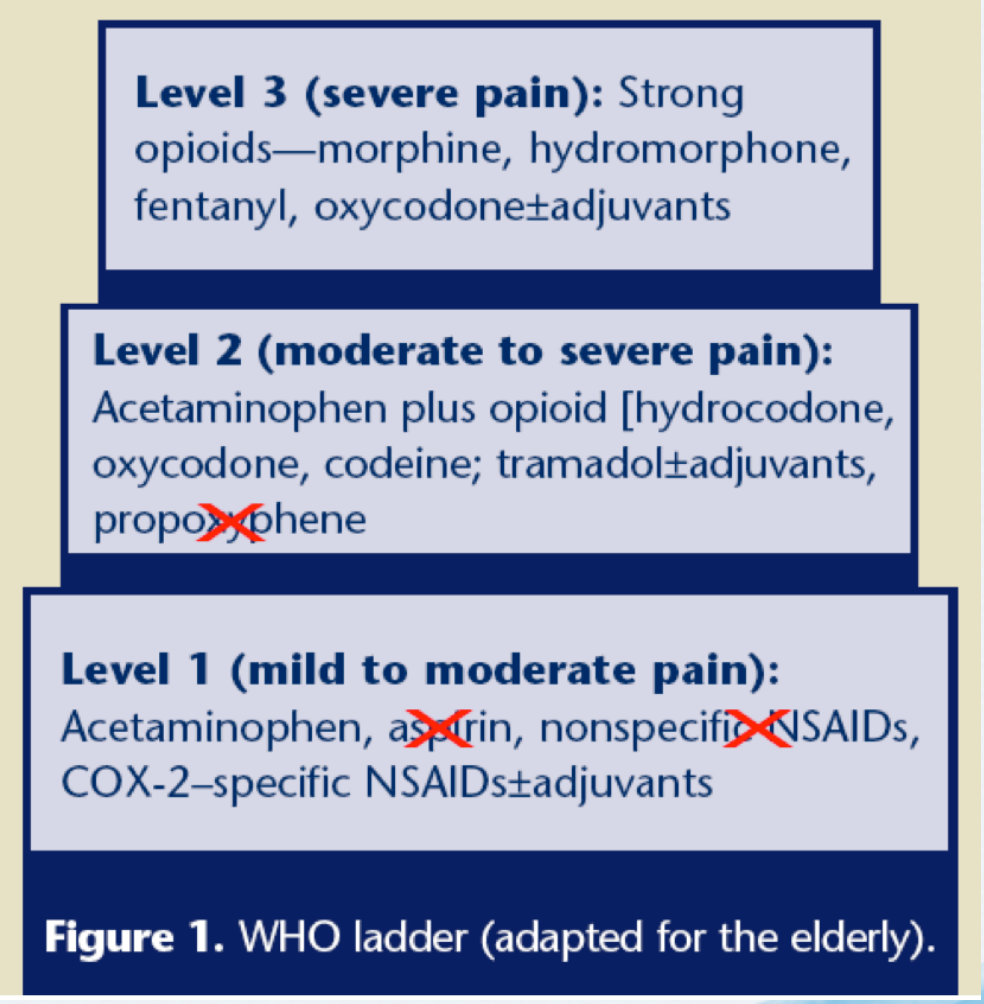
Pain Management in Elderly: Pharmacological Therapy Consideration

- Age-related changes in metabolism
  - Changes in renal and hepatic function
  - Changes in gastrointestinal function
  - Changes in body fat/muscle composition

Increase risk of side effects and analgesics related complications

START LOW, GO SLOW...

WHO Ladder Adapted for Elderly



Argoff, Charles. Chronic Pain Management in The Elderly. Supplement for Geriatrics. New York : November 2005.

Acetaminophen

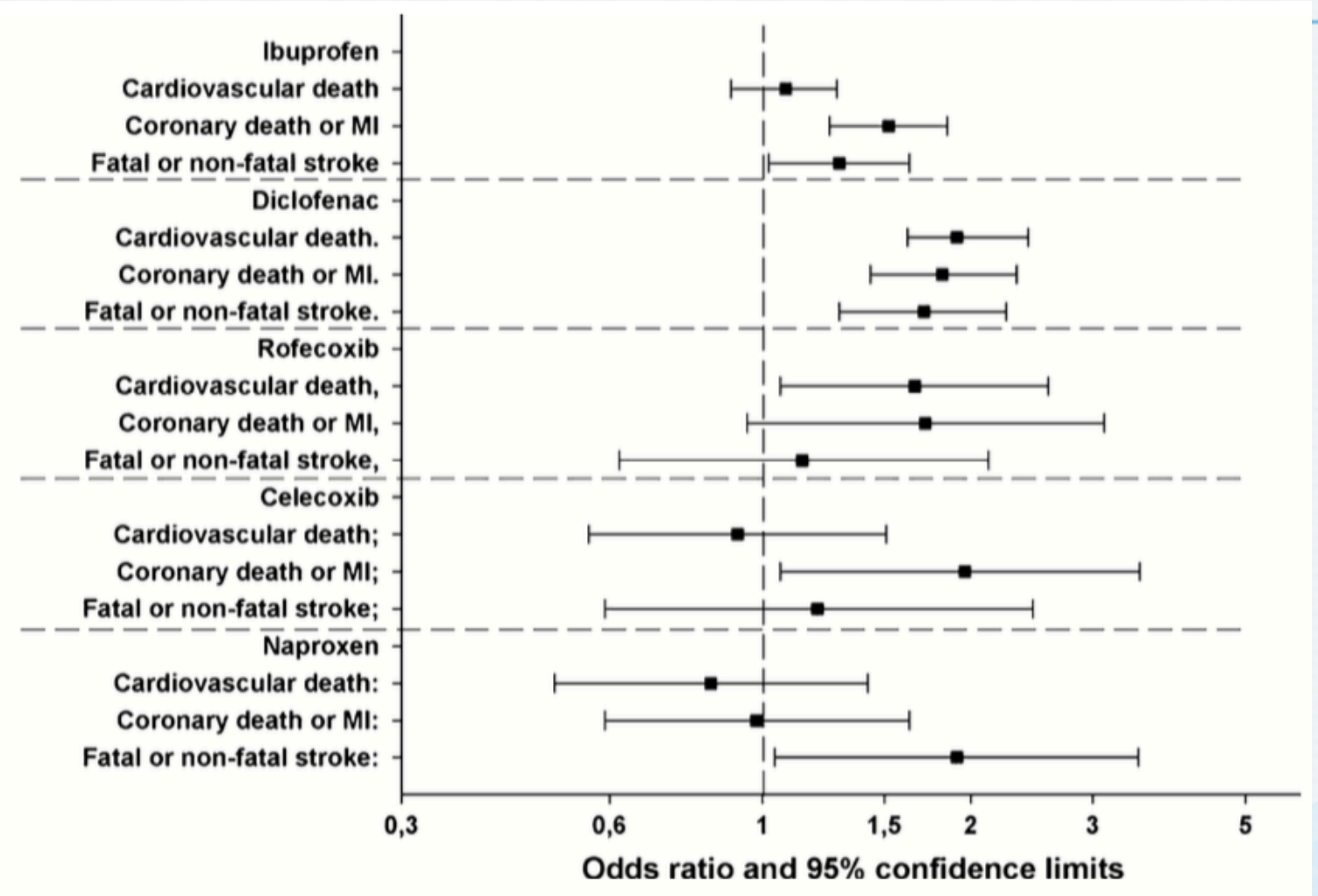
- First choice for mild to moderate chronic musculoskeletal pain
- Maximum dose: 4g/day – included “hidden source”
- Absolute contraindication: liver failure
- Cautions: hepatic insufficiency, chronic alcohol abuse or dependence

NSAIDs

Organ System, Therapeutic Category, Drugs	Rationale	Recommendation	Quality of Evidence	Strength of Recommendation
Non-cyclooxygenase-selective NSAIDs, oral: Aspirin >325 mg/d Diclofenac Diflunisal Etodolac Fenoprofen Ibuprofen Ketoprofen Meclofenamate Mefenamic acid Meloxicam Nabumetone Naproxen Oxaprozin Piroxicam Sulindac Tolmetin	Increased risk of gastrointestinal bleeding or peptic ulcer disease in high-risk groups, including those aged >75 or taking oral or parenteral corticosteroids, anticoagulants, or antiplatelet agents; use of proton-pump inhibitor or misoprostol reduces but does not eliminate risk. Upper gastrointestinal ulcers, gross bleeding, or perforation caused by NSAIDs occur in approximately 1% of patients treated for 3–6 months and in ~2–4% of patients treated for 1 year; these trends continue with longer duration of use	Avoid chronic use, unless other alternatives are not effective and patient can take gastroprotective agent (proton-pump inhibitor or misoprostol)	Moderate	Strong
Indomethacin	Indomethacin is more likely than other NSAIDs to have adverse CNS effects. Of all the NSAIDs, indomethacin has the most adverse effects.	Avoid	Moderate	Strong
Ketorolac, includes parenteral	Increased risk of gastrointestinal bleeding, peptic ulcer disease, and acute kidney injury in older adults			

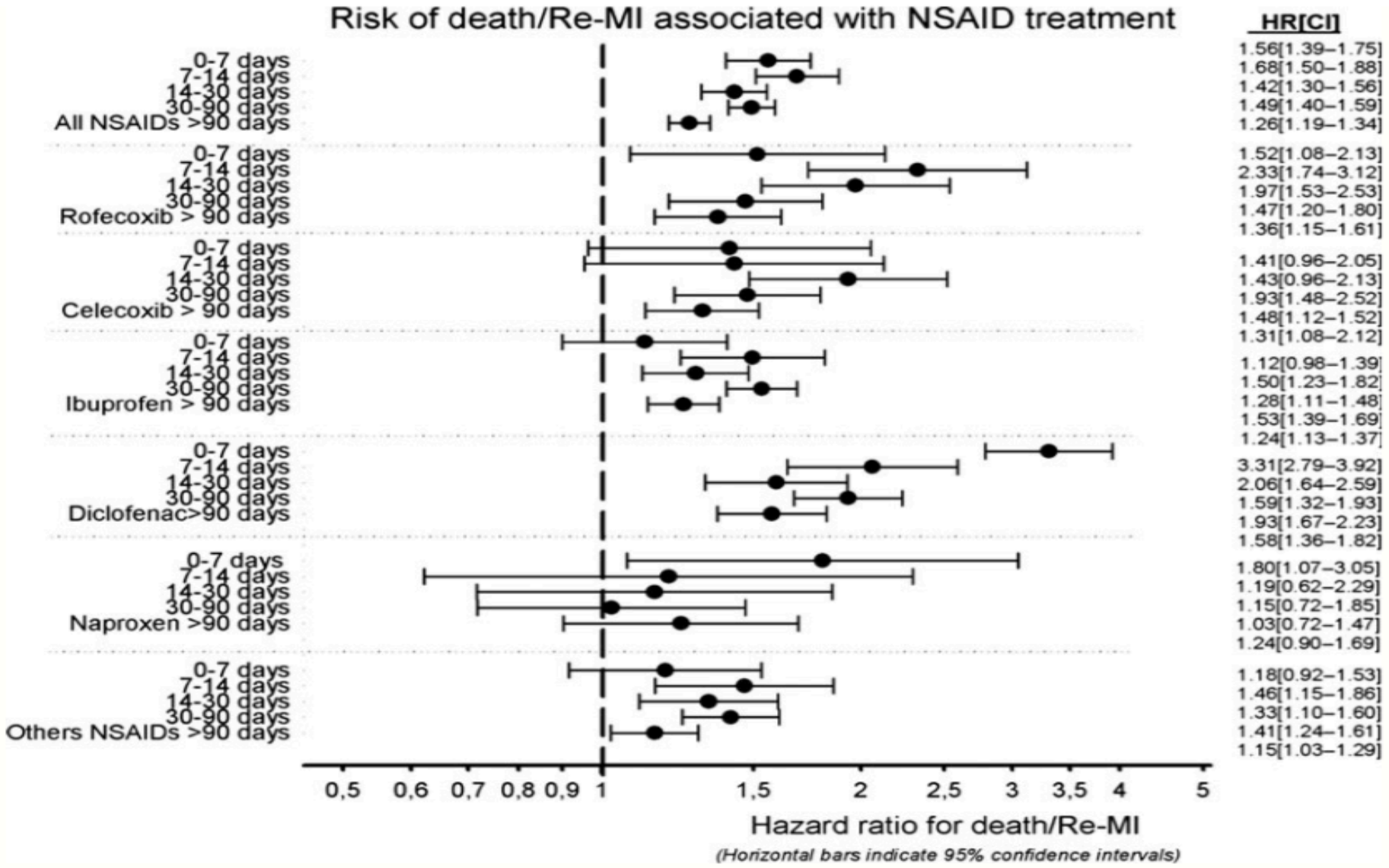
American Geriatrics Society 2015: Updated Beers Criteria for Potentially Inappropriate Medication Use in Older Adults
J Am Geriatr Soc 63:2227-2246

Cardiovascular Risk Associated with NSAIDs



Olsen, A S, Fosbet, EL, Gislason, GH. The impact of NSAID Treatment on Cardiovascular Risk-Insight from Danish Observational Data. Basic & Clinical Pharmacology & Toxicology 2014;115:179-184

Cardiovascular Risk Associated with NSAIDs



Olsen, A S, Fosbet, EL, Gislason, GH. The impact of NSAID Treatment on Cardiovascular Risk-Insight from Danish Observational Data. Basic & Clinical Pharmacology & Toxicology 2014;115:179-184

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FOR IMMEDIATE RELEASE

More Evidence Arthritis/Pain Relieving Drugs May Contribute to Stroke Death

MINNEAPOLIS – Commonly prescribed, older drugs for arthritis and pain may increase the risk of death from stroke, according to a study published in the November 5, 2014, online issue of Neurology®, the medical journal of the American Academy of Neurology. Stroke is the fourth leading cause of death in the United States, according to the Centers for Disease Control and Prevention.

The drugs examined in the study, called COX-2 inhibitors, include older drugs diclofenac, etodolac, nabumeton and meloxicam, as well as newer drugs called coxibs, including celecoxib and rofecoxib. COX-2 inhibitors are selective nonsteroidal anti-inflammatory drugs (NSAIDs). The study also looked at non-selective NSAIDs, which include common pain relievers such as ibuprofen and naproxen.

"While newer versions of these COX-2 inhibitors drugs have been pulled off shelves, older ones are still frequently prescribed," said study author Morten Schmidt, MD, of Aarhus University Hospital in Aarhus, Denmark. "Our study provides further important evidence solidifying the risks of certain arthritic pain relievers and death from stroke."

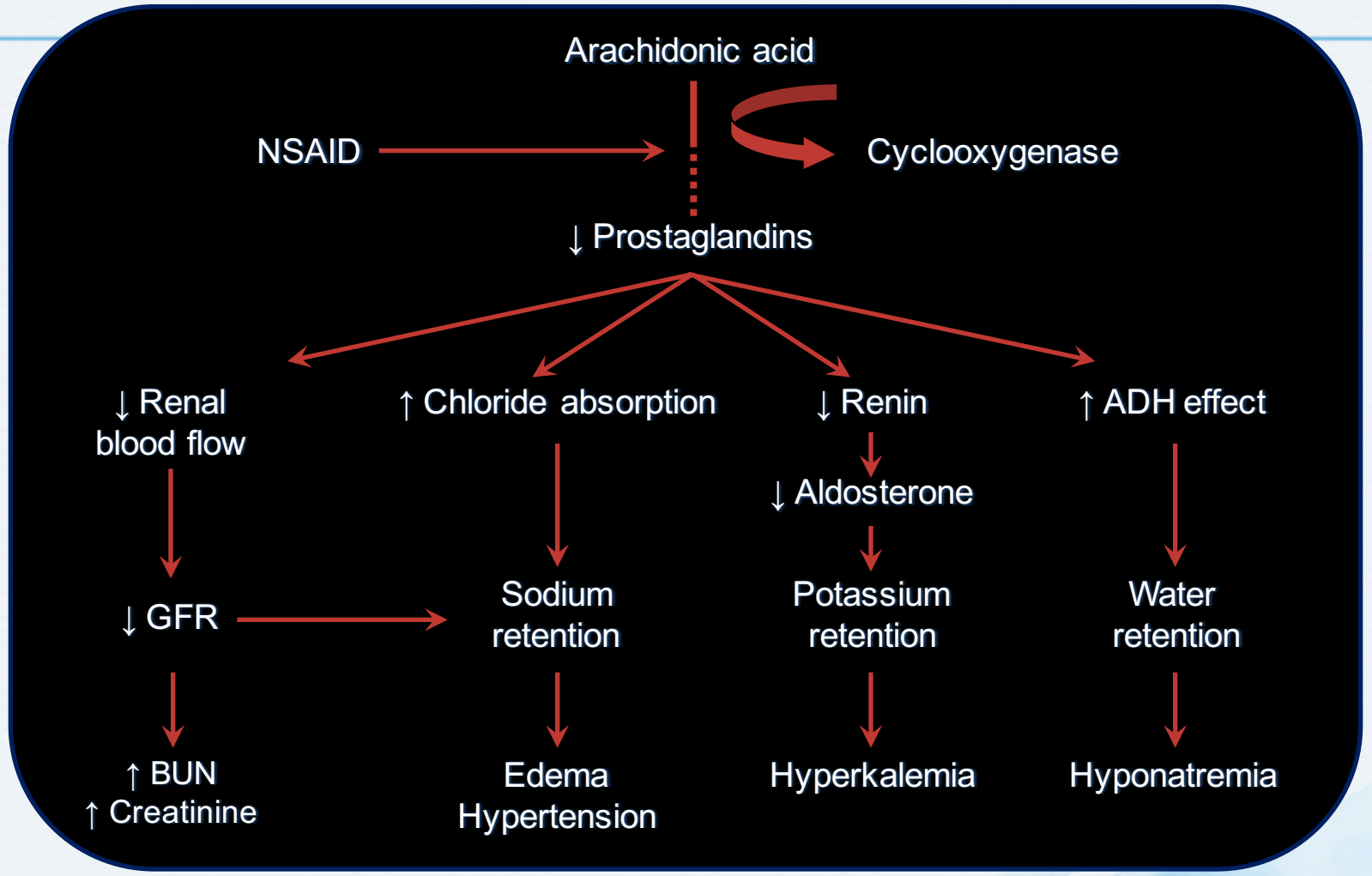
For the study, researchers looked at records of 100,243 people hospitalized for a first stroke in Denmark between 2004 and 2012 and deaths within one month after the stroke. Researchers looked at whether participants were current, former, or non-users of these drugs within two months of the stroke. If they were current users, researchers noted whether people were new users who had just started taking the drug for the first time or were long-term users. They looked at newer generation COX-2 inhibitors, older generation COX-2 inhibitors, and non-selective NSAIDS.

Overall, people who were current users of COX-2 inhibitors were 19 percent more likely to die after stroke than people who did not take the drugs (10.4 percent versus 8.7 percent). New users of the older COX-2 drugs were 42 percent more likely to die from stroke than those who were not taking the drugs. Those taking etodolac were 53 percent more likely to die from stroke.

AMERICAN ACADEMY OF NEUROLOGY®

American Academy of Neurology, November 2014.
https://www.aan.com/PressRoom/home/PressRelease/1316

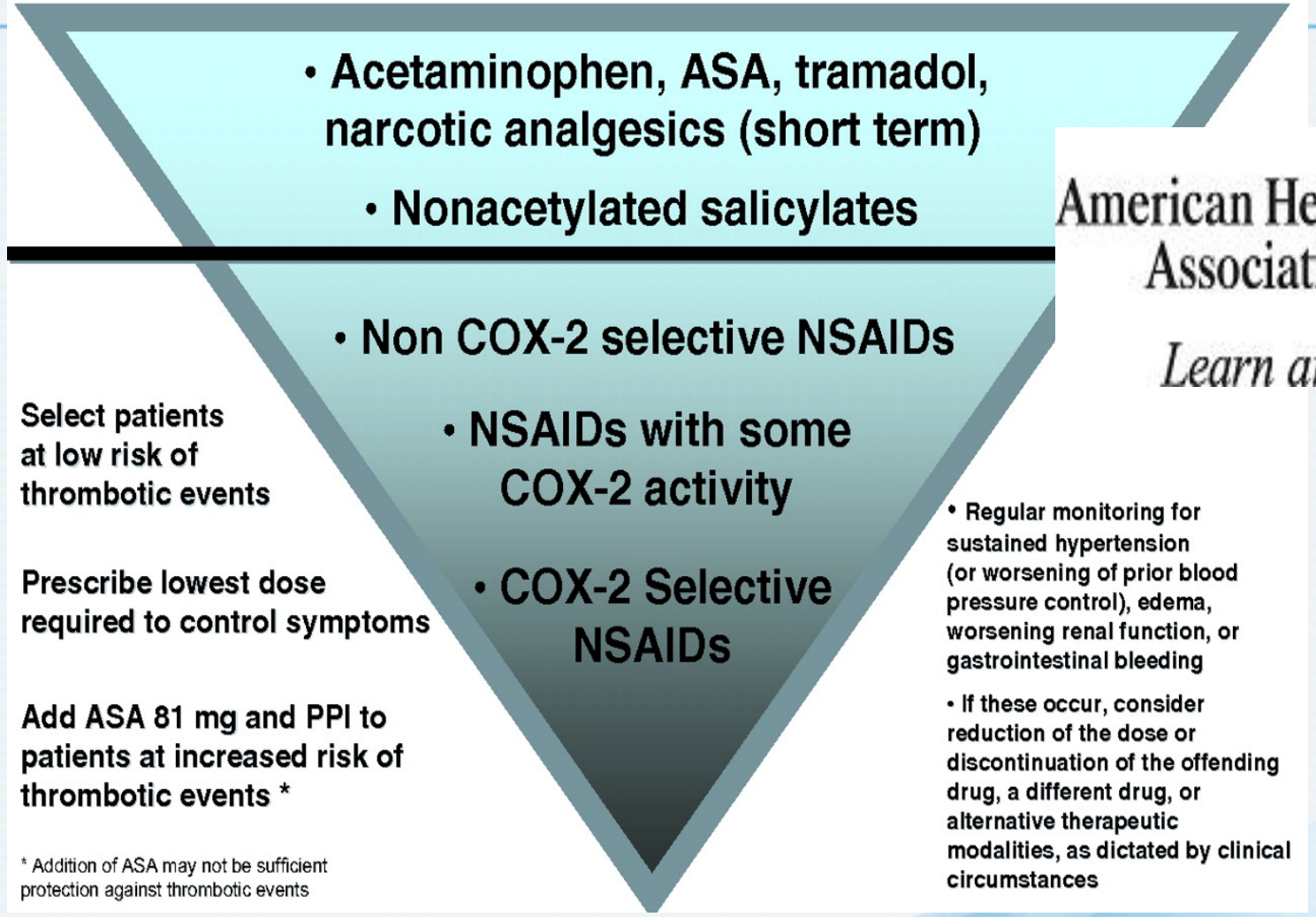
Renal Effects Associated With NSAID-Induced Prostaglandin Inhibition



ADH=antidiuretic hormone; BUN=blood urea nitrogen; GFR=glomerular filtration rate.

Adapted with permission from Aronoff GR. *J Rheumatol*. 1992;19(suppl 36):25-31.

Stepped Care Approach to Pharmacologic Therapy for Musculoskeletal Symptoms With Known Cardiovascular Disease or Risk Factors for Ischemic Heart Disease



American Heart Association®

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Antman, EM et al. Use of nonsteroidal antiinflammatory drugs: an update for clinicians: a scientific statement from the American Heart Association. *Circulation* 2007 Mar 27;115(12):1634-42.

ORIGINAL ARTICLE

JBMR®

Long-Term Proton Pump Inhibitor Therapy and Falls and Fractures in Elderly Women: A Prospective Cohort Study

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ABSTRACT

Proton pump inhibitors (PPIs) are widely used in the elderly. Recent studies have suggested that long-term PPI therapy is associated with fractures in the elderly, however the mechanism remains unknown. We investigated the association between long-term PPI therapy $\geq$1 year and fracture risk factors including bone structure, falls, and balance-related function in a post hoc analysis of a longitudinal population-based prospective cohort of elderly postmenopausal women and replicated the findings in a second prospective study of falling in elderly postmenopausal women. Long-term PPI therapy was associated with increased risk of falls and fracture-related hospitalizations; adjusted odds ratio (AOR) 2.17; 95% CI, 1.25–3.77; $p = 0.006$ and 1.95; 95% CI, 1.20–3.16; $p = 0.007$, respectively. In the replication study, long-term PPI use was associated with an increased risk of self-reported falling; AOR, 1.51; 95% CI, 1.00–2.27; $p = 0.049$. No association of long-term PPI therapy with bone structure was observed; however, questionnaire-assessed falls-associated metrics such as limiting outdoor activity ($p = 0.002$) and indoor activity ($p = 0.001$) due to fear of falling, dizziness ($p < 0.001$) and numbness of feet ($p = 0.017$) and objective clinical measurement such as Timed Up and Go ($p = 0.002$) and Romberg eyes closed ($p = 0.025$) tests were all significantly impaired in long-term PPI users. Long-term PPI users were also more likely to have low vitamin B12 levels than non-users (50% versus 21%, $p = 0.003$). In conclusion, similar to previous studies, we identified an increased fracture risk in subjects on long-term PPI therapy. This increase in fracture risk in elderly women, already at high risk of fracture, appears to be mediated via increased falls risk and falling rather than impaired bone structure and should be carefully considered when prescribing long-term PPI therapy.

KEY WORDS: PROTON PUMP INHIBITOR THERAPY; ADVERSE EVENTS; FALLS; FRACTURE; VITAMIN B12

Recommendation on NSAIDs & Selective COX-2 Inhibitors

- Use with caution after other safer treatments have not provided sufficient pain relief
- Should use lowest dose for short duration
- Should be co-prescribed with proton-pump inhibitor
- Monitor routinely for
  - gastrointestinal, renal, cardiovascular side effects
  - drug–drug and drug–disease interactions

OPIOIDS in Older Persons

2002: 'for many older patients, chronic opioid therapy may have fewer life-threatening risks than long-term daily use of NSAIDs'

2009: 'NSAIDs worsen CHF, hypertension, ischemia, and MI, and should not be used in patients > 75 years of age

Opioids: 'lack of organ damaging effects'

(gastro-intestinal, cardiovascular, renal)

2012 & 2015: Opioids together with PPIs are related with the risk of fall

1. JAGS Panel on Persistent Pain in Older Persons. The management of persistent pain in older persons. *J Am Geriatr Soc* 2002 Jun;50(6 Suppl):S205-24.
2. American Geriatrics Society Panel on Pharmacological Management of Persistent Pain in Older Persons. Pharmacological management of persistent pain in older persons. *J Am Geriatr Soc* 2009 Aug;57(8):1331-46.

Clinical outcomes of the use of opioids in elderly patients with impaired renal function

Opioid	T ½	T1/2 metabolites	Clinical Outcome	Recommendation
Morphine	↑	↑↑	Increases active metabolites M3G and M6G may lead to long lasting respiratory depression	Dosage ↓
Oxycodone	↑	↑	Clearly reduces renal clearance of parent compound and metabolites	Dosage ↓
Hydromorphone	↑	↑↑	Metabolites accumulate	Dosage ↓
Fentanyl TD	↑	↑	Decreases renal clearance	Dosage ↓
Buprenorphine	=	=	No clinically relevant change	Adjust dosage
Methadone	↑	↑	Not extensively evaluated in patients with renal impairment – use with caution	Dosage ↓

Gianni W, et al. Opioids for the treatment of Chronic Non-Cancer Pain in Older People. Drugs Aging 2009;1: 63-73

Effect of reduced hepatic function on pharmacokinetics of opioids

Opioid	T ½	T1/2 metabolites	Finding	Recommendation
Morphine	↑	↓	M6G ↓	Dosage ↓
Oxycodone	↑	↑	No data available	Dosage ↓
Hydromorphone	?	?	No data available	Dosage ↓
Fentanyl TD	↑	?	No data available	Dosage ↓
Buprenorphine	↑	↓	Low activity metabolites	Dosage ↓
Methadone	↑	?	No data available	Dosage ↓

Gianni W, et al. Opioids for the treatment of Chronic Non-Cancer Pain in Older People. Drugs Aging 2009;1: 63-73

Tramadol

- Mild to moderate pain
- Dual effect
  - Mu receptor
  - Serotonine and Noradrenaline reuptake inhibitor
- Increases risk of seizure
  - Caution for patients with brain lesion

Opioids Side Effect Management

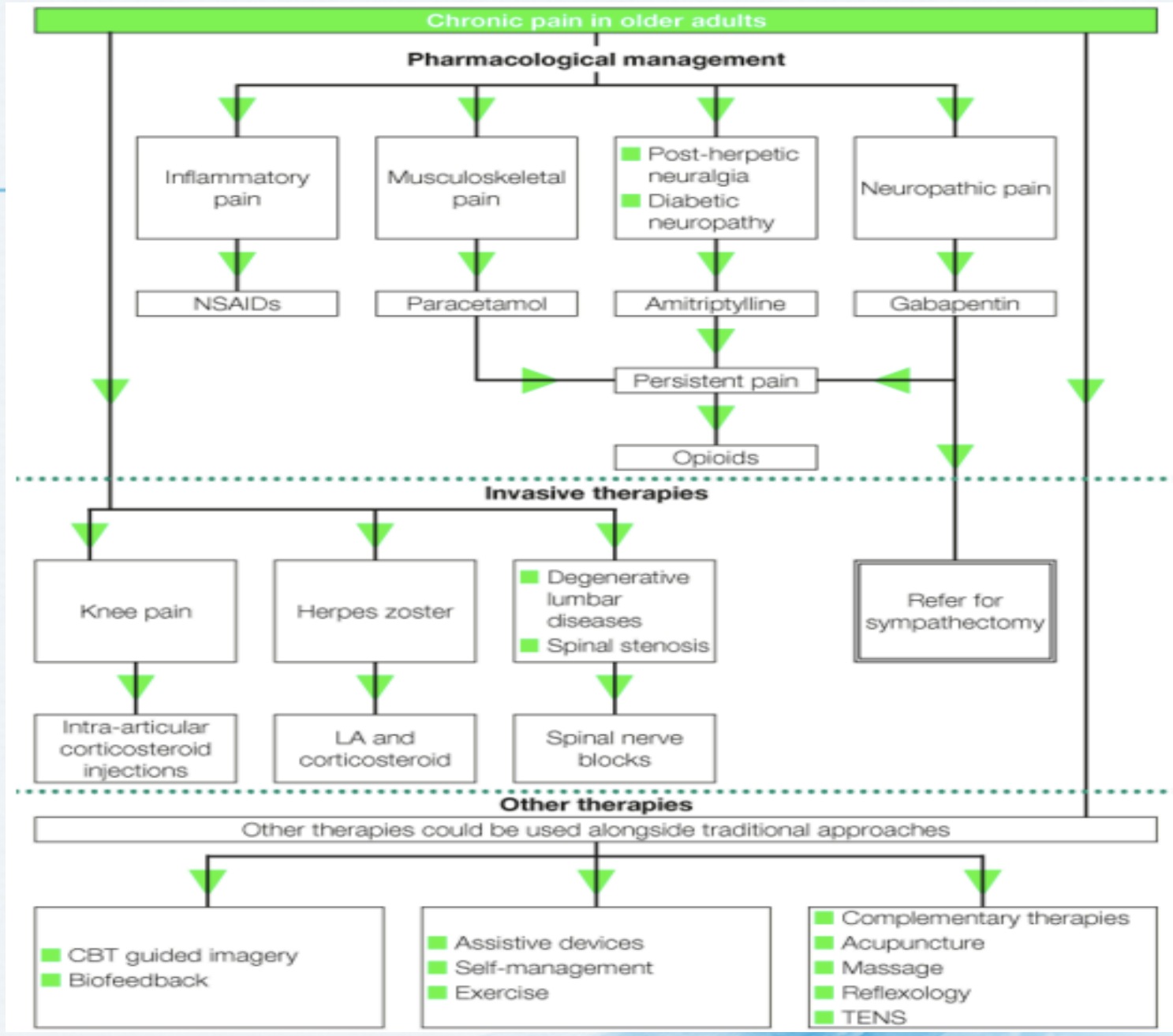
SYMPTOM	TREATMENT
Constipation	Bowel stimulants, stool softeners, enemas
Nausea	Antiemetics
Fatigue/sedation	Reduce dose , add non sedating co-analgesics or stimulants
Dizziness/confusion	Antivertiginous agents
Central Nervous System function/Myoclonus	Reduce dose, or add benzodiazepines
Itching	Antipruritic therapy
Urinary retention (rare)	Rotate to different opioids; discuss catheterization
Respiratory depression (rare)	Care with opioid naïve patient; avoid medication with long half-life during rapid titration; care with other medication such as benzodiazepines

Tenzer P, Pain in the Elderly. Pain Management Today 2007; Vol 7(1) http://www.painedu.org

Adjuvant Analgesics

Antidepressants	
TCAs	Contraindicated for elderly due to its anticholinergic side effects, sedation, induced cardiac arrhytmias and glaucoma Nortryptylline is safer
SSRI	The evidence of pain relieve is controversial
SNRI	Better efficacy and tolerability
Antiepileptics	
Gabapentinoids	Dose titration is needed Dose adjustment in renal disease is needed
Topical treatments	
NSAIDs	Effective to reduce pain; reduce the incidence of systemic adverse effects
Lidocaine	Third line treatment of PHN Few side effects
Capsaicin	Effective for PHN, some patients can not tolerate the intense burning sensation after application

British Geriatric Society, Guidance on the management of pain in older people. Age and Ageing 2013;42:i1-i57


Chronic pain in older adults
Pharmacological management
Inflammatory pain
Musculoskeletal pain
Post-herpetic neuralgia
Diabetic neuropathy
Neuropathic pain
NSAIDs
Paracetamol
Amitriptylline
Gabapentin
Persistent pain
Opioids
Invasive therapies
Knee pain
Herpes zoster
Degenerative lumbar diseases
Spinal stenosis
Refer for sympathectomy
Intra-articular corticosteroid injections
LA and corticosteroid
Spinal nerve blocks
Other therapies
Other therapies could be used alongside traditional approaches
CBT guided imagery
Biofeedback
Assistive devices
Self-management
Exercise
Complementary therapies
Acupuncture
Massage
Reflexology
TENS

Expectation of Therapy

- Patient education about **realistic pain relief** and combination therapy with pharmacologic and nonpharmacologic interventions will achieve *acceptable pain control and improve physical, emotional, psychological, and social well-being* in older adults with chronic pain.

Conclusion

- Pharmacological treatment for chronic pain in elderly needs a careful risk and benefit consideration
- NSAIDs are not only related with GI tract complication, but also renal and cardiovascular events
- Opioids compared with NSAIDs may have a better safety profile but careful monitoring is still needed
- Adjuvant analgesics need to be carefully monitored for side effects
- “START LOW GO SLOW”
- Multidisciplinnary team approach in the management of chronic pain in elderly is essential

TERIMA KASIH