A SELECTION OF TEN CURRENT READINGS ON TOPICS RELATED TO THIS FAMILY PRACTICE SKILLS COURSE 78 – GDFM ENHANCED PROGRAMME – CHRONIC DISEASE MANAGEMENT

Some are available as free full text and some requiring papyemnt
Selection of readings made by A/Prof Goh Lee Gan

READING 1 – BLOOD PRESSURE GOALS IN PATIENTS WITH CHRONIC KIDNEY DISEASE (CKD)

Chang AR, Lóser M, Malhotra R, Appel LJ. Blood Pressure Goals in Patients with CKD: A Review of Evidence and Guidelines. Clinical Journal of the American Society Nephrology. 2019 Jan 7; 14(1):161-9.

Doi: 10.2215/CJN.07440618. Epub 2018 Nov 19. Review. PubMed
PMID: 30455322. [Payment required]

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ABSTRACT

Hypertension affects the vast majority of patients with CKD and increases the risk of cardiovascular disease, end-stage kidney disease (ESKD), and death.

Over the past decade, a number of hypertension guidelines have been published with varying recommendations for blood pressure (BP) goals in patients with CKD.

Most recently, the American College of Cardiology/American Heart Association 2017 hypertension guidelines set a BP goal of <130/80 mm Hg for patients with CKD and others at elevated cardiovascular risk.

These guidelines were heavily influenced by the landmark Systolic Blood Pressure Intervention Trial (SPRINT), which documented that an intensive BP goal to a systolic BP <120 mm Hg decreased the risk of cardiovascular disease and mortality in nondiabetic adults at high cardiovascular risk, many of whom had CKD; the intensive BP goal did not retard CKD progression.

It is noteworthy that SPRINT measured BP with automated devices (Five-minute wait period, average of three readings) often without observers, a technique that potentially results in BP values that are lower than what is typically measured in the office. Still, results from SPRINT along with long-term follow-up data from the Modification of Diet in Renal Disease and the African American Study of Kidney Disease and Hypertension suggest that a BP goal <130/80 mm Hg will reduce mortality in patients with CKD.

Unfortunately, data are more limited in patients with diabetes or stage 4-5 CKD. Increased adverse events, including electrolyte abnormalities and decreased eGFR, necessitate careful laboratory monitoring. In conclusion, a BP goal of <130/80 is a reasonable, evidence-based BP goal in patients with CKD.

Implementation of this intensive BP target will require increased attention to measuring BP accurately, assessing patient preferences and concurrent medical conditions, and monitoring for adverse effects of therapy.

READING 2 – ANTIHYPERTENSIVE THERAPY IN NONDIABETIC CHRONIC KIDNEY DISEASE

Der Mesropian PJ, Shaikh G, Torres EC, Bilal A, Mathew RO. Antihypertensive therapy in nondiabetic chronic kidney disease: a review and update. Journal of the American Society of Hypertension. 2018 Mar 1;12(3):154-81.

Doi: 10.1016/j.jash.2018.01.005. Epub 2018 Jan 31. Review. PubMed
PMID: 29396103. [Payment required]

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ABSTRACT
Hypertension is an important contributor to progression of nondiabetic chronickidney disease (CKD).

Compelling observational evidence indicates that the divergence of blood pressure (BP) away from an ideal range in either direction is associated with a progressive rise in the risk of mortality and cardiovascular and renal disease progression.

To date, various clinical trials and meta-analyses examining strict versus less intensive BP control in nondiabetic CKD have not conclusively demonstrated a renal advantage of one BP-lowering approach over another, except in certain subgroups such as proteinuric patients where evidence is circumstantial. As recent data have come to light suggesting that intensive BPcontrol yields superior survival and cardiovascular outcomes in patients at high risk for cardiovascular disease, interest in the prospect of whether such benefit extends to individuals with CKD has surged.

This review is a comprehensive analysis of antihypertensive literature in nondiabetic renal disease, with aparticular emphasis on BP target.

Published by Elsevier Inc.

READING 3 – BARRIERS TO INSULIN THERPY AND APPROACHES TO OVERCOME THEM

Russell-Jones D, Pouwer F, Khunti K. Identification of barriers to insulin therapy and approaches to overcoming them. Diabetes Obesity and Metabolism. 2018 Mar; 20(3):488-96.

Doi: 10.1111/dom.13132. Epub 2017 Nov 22. Review. PubMed
PMID: 29053215; PubMed Central PMCID: PMC5836933. [Free full text]

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ABSTRACT
Poor glycaemic control in type 2 diabetes (T2D) is a global problem despite the availability of numerous glucose-lowering therapies and clear guidelines for T2D management.

Tackling clinical or therapeutic inertia, where the person with diabetes and/or their healthcare providers do not intensify treatment regimens despite this being appropriate, is key to improving patients' long-term outcomes.

This gap between best practice and current level of care is most pronounced when considering insulin regimens, with studies showing that insulin initiation/intensification is frequently and inappropriately delayed for several years.

Patient- and physician-related factors both contribute to this resistance at the stages of insulin initiation, titration and intensification, impeding achievement of optimal glycaemic control.

The present review evaluates the evidence and reasons for this delay, together with available methods for facilitation of insulin initiation or intensification.

READING 4 – INSULIN THERAPY INCREASES CARDIOVASCULAR RISK IN TYPE 2DIABETES MELLITUS

Herman ME, O'Keefe JH, Bell DS, Schwartz SS. Insulin therapy increases cardiovascular risk in type 2 diabetes. Progress in cardiovascular diseases. 2017 Nov 1;60(3):422-34.

Doi: 10.1016/j.pcad.2017.09.001. Epub 2017 Sep 25. Review. PubMed
PMID: 28958751. [Payment required]

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ABSTRACT
Insulin therapy increased cardiovascular (CV) risk and mortality among type 2 diabetes (T2D) patients in several recently reported clinical outcomes trials. To assess whether this association is causative or coincidental,

PubMed searches were used to query the effects of insulin therapy for T2D on CV health and longevity from large-scale outcomes trials, meta-analyses, and patient registry studies, as well as basic research on insulin's direct and pleiotropic actions.

Although several old studies provided conflicting results, the majority of large observational studies show strong dose-dependent associations for injected insulin with increased CV risk and worsened mortality.

Insulin clearly causes weight gain, recurrent hypoglycemia, and, other potential adverse effects, including iatrogenic hyperinsulinemia.

This over-insulinisation with use of injected insulin predisposes to inflammation, atherosclerosis, hypertension, dyslipidemia, heart failure (HF), and arrhythmias. These associations support the findings of large-scale evaluations that strongly suggest that insulin therapy has a poorer short- and long-term safety profile than that found to many other anti-T2D therapies.

The potential adverse effects of insulin therapy should be weighed against proven CV benefits noted for selecting other therapies for T2D as reported in recent large randomised controlled trials.

READING 5 – OBESITY AND DIABETES

Verma S, Hussain ME. Obesity and diabetes: an update. Diabetes & Metabolic Syndrome: Clinical Research & Reviews. 2017 Jan 1;11(1):73-9.

doi: 10.1016/j.dsx.2016.06.017. Epub 2016 Jun 17. Review. PubMed
PMID: 27353549. [Payment required]

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ABSTRACT
The twin epidemic of obesity and diabetes is a major crisis globally. Severalepidemiologic studies reveal the parallel escalation of obesity and diabetes.

The term 'diabesity' expresses their close relationship to each other, wherein both these metabolic disorders are characterised by defects of insulin action. The pathophysiology connecting obesity and diabetes is chiefly attributed to two factors: insulin resistance and insulin deficiency.

Recent years have seen an increasing body of work on the following metabolic defects common to both obesity and diabetes such as, impaired tissue perfusion, sleep disturbances, androgen dysfunction, altered Vitamin D levels and GI stress.

The scope of this review is to present the most widely accepted theories that link the two diseases, provide an update on some proposed unifying metabolic defects and highlight current and future prevention and management strategies.

READING 6 – LIFESTYLE INTERVENTIONS FOR PATIENTS WITH NONALCOHOLIC FATTY LIVER DISEASE (NAFLD)

Zou TT, Zhang C, Zhou YF, Han YJ, Xiong JJ, Wu XX, Chen YP, Zheng MH. Lifestyle interventions for patients with nonalcoholic fatty liver disease: a network meta-analysis. European journal of gastroenterology & hepatology. 2018 Jul 1;30(7):747-55.

Doi: 10.1097/MEG.0000000000001135. Review. PubMed
PMID: 29683979. [Payment required]

Zou TT(1)(2), Zhang C(3), Zhou YF(1)(4), Han YJ(1)(4), Xiong JJ(1)(4), WuXX(1)(5), Chen YP(1)(6), Zheng MH(1)(6-7).

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ABSTRACT
Lifestyle interventions remain the first-line therapy for nonalcoholic fatty liver disease (NAFLD).

This study aims to evaluate the individual impact of exercise and/or dietary interventions on the level of alanine aminotransferase(ALT), aspartate aminotransferase (AST), homeostasis model of assessment for insulin resistance index (HOMA-IR), and BMI.

Randomised-controlled trials from patients diagnosed with NAFLD were included in the meta-analysis if they reported the associations between changes in ALT, AST, HOMA-IR, or BMI and types of lifestyle interventions. Nineteen eligible articles were included.

Compared with observation, aerobic exercise training (AEx) plus diet [weighted mean difference (WMD) =-25.85; 95% confidence interval (CI): -43.90 to -7.80], AEx (WMD=-8.81; 95%CI: -20.22-2.60) and diet (WMD=-11.85; 95% CI: -47.65-24.95) showed significant efficacy in the improvement of ALT levels. Also AST, AEx plus diet showed asignificant tendency to reduce AST levels. In addition, progressive resistance training (WMD=-1.70; 95% CI: -5.61-2.21) led to the most obvious reduction inHOMA-IR compared with observation, but appeared to show no significant effect in BMI (WMD=0.27; 95% CI: -0.48 to -0.07), whereas AEx plus diet (WMD=-0.96; 95% CI:-1.54 to -0.38 and WMD=-1.96; 95% CI: -2.79 to -1.12) showed great efficacy both in the improvement of HOMA-IR and BMI.

AEx plus diet is the most effective intervention in the management of patients with NAFLD. Dietary intervention maybe more effective in the improvements of aminotransferases, whereas exercise shows superiority in improving insulin sensitivity and reduction of BMI.

READING 7 – SYNERGISTIC INCREASE IN CARDIOVASCULAR RISK IN DIABETES MELLITUS WITH NONALCOHOLIC FATTY LIVER DISEASE

Zhou YY, Zhou XD, Wu SJ, Hu XQ, Tang B, Poucke SV, Pan XY, Wu WJ, Gu XM, Fu SW, Zheng MH. Synergistic increase in cardiovascular risk in diabetes mellitus with nonalcoholic fatty liver disease: a meta-analysis. European Journal of Gastroenterology & Hepatology. 2018 Jun 1; 30(6):631-6.

Doi: 10.1097/MEG.0000000000001075. Review. PubMed
PMID: 29351115. [Payment required]

Zhou YY(1), Zhou XD(2), Wu SJ(2), Hu XQ(1), Tang B(1), Poucke SV(3), Pan XY(4),Wu WJ(4), Gu XM(4), Fu SW(1), Zheng MH(5)(6).

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ABSTRACT
BACKGROUND: Nonalcoholic fatty liver disease (NAFLD) has been linked to an increased risk of cardiovascular disease (CVD). To explore the impact of diabetesmellitus (DM) as a cardiovascular risk factor, this meta-analysis quantitatively assessed the association of NAFLD and CVD in diabetic patients.

METHODS: PubMed, EMBASE, and the Cochrane Library database were analysed until the end of March 2017. Original studies analysing the association between NAFLD and cardiovascular risk factors in the diabetic population were included. The available data related to outcome were extracted for the effect estimate using a random-effects model. The quality of the included studies was assessed using the Newcastle-Ottawa Quality Assessment Scale.

RESULTS: Of the 770 initially identified studies, 11 studies involving 8346 patients were finally included. The Newcastle-Ottawa Quality Assessment Scalescores suggested that the studies included were of high quality. The pooled effects estimate showed that diabetic patients with NAFLD showed a two times increased risk for CVD compared with patients without NAFLD (odds ratio=2.20, 95%confidence interval: 1.67-2.90). Subgroup analysis also yielded a markedly increased risk, with odds ratio (95% confidence interval) values of 2.28(1.61-3.23) and 1.90 (1.48-2.45) in cross-sectional and cohort studies,respectively.

CONCLUSION: This is the first meta-analysis investigating the relationship between NAFLD and CVD independent of the impact of DM. Our findings suggested that NAFLD increases the risk of CVD in populations with comparable DM profiles. Diabetic patients diagnosed with NAFLD might benefit from a more early cardiovascular risk assessment, thereby reducing CVD morbidity and mortality.

DOI: 10.1097/MEG.0000000000001075
PMID: 29351115 [Indexed for MEDLINE]

READING 8 – CARDIOVASCULAR SAFETY OF NON-INSULIN PHARMACOTHERAPY FOR TYPE 2 DIABETES MELLITUS

Xu J, Rajaratnam R. Cardiovascular safety of non-insulin pharmacotherapy for type 2 diabetes. Cardiovascular Diabetology. 2017 Feb 2;16(1):18.

Doi: 10.1186/s12933-017-0499-5. Review. PubMed PMID: 28148253; PubMed Central PMCID: PMC5288947 [Free full text].

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ABSTRACT
Patients with type 2 diabetes mellitus have a twofold increased risk of cardiovascular mortality compared with non-diabetic individuals.

There is a growing awareness that glycemic efficacy of anti-diabetic drugs does not necessarily translate to cardiovascular safety.

Over the past few years, there has been a number of trials evaluating the cardiovascular effects of anti-diabetic drugs.

In this review, we seek to examine the cardiovascular safety of these agents in major published trials.

Metformin has with-stood the test of time and remains the initial drug of choice. The sulfonylureas, despite being the oldest oral anti-diabetic drug, has been linked to adverse cardiovascular events and are gradually being out-classed by the various other second-line agents. The glitazones are contraindicated in heart failure. The incretin-based drugs have been at the fore-front of this era of cardiovascular safety trials and their performances have been reassuring, whereas the meglitinides and the alpha-glucosidase inhibitors still lack cardiovascular outcomes data. The sodium glucose cotransporter-2 inhibitors are an exciting new addition that has demonstrated a potential for cardiovascular benefit.

Many of the currently available oral anti-diabetic agents have clinically relevant cardiovascular effects. The optimal approach to the reduction of cardiovascular risk in diabetic patients should focus on aggressive management of the standard cardiovascular risk factors rather than purely on intensive glycemic control.

READING 9 – MANAGEMENT OF GOUT AND HYPERURICEMIA

Yu KH, Chen DY, Chen JH, Chen SY, Chen SM, Cheng TT, Hsieh SC, Hsieh TY, HsuPF, Kuo CF, Kuo MC, Lam HC, Lee IT, Liang TH, Lin HY, Lin SC, Tsai WP, Tsay GJ,Wei JC, Yang CH, Tsai WC. Management of gout and hyperuricemia: Multidisciplinaryconsensus in Taiwan. International Journalof Rheumatic Disease. 2018 Apr; 21(4):772-87.

Doi:10.1111/1756-185X.13266. Epub 2018 Jan 24. Review. PubMed
PMID: 29363262 [Payment required].

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ABSTRACT
Gout is an inflammatory disease manifested by the deposition of monosodium urate(MSU) crystals in joints, cartilage, synovial bursa, tendons or soft tissues. Gout is not a new disease, which was first documented nearly 5,000 years ago.

The prevalence of gout has increased globally in recent years, imposing great disease burden worldwide. Moreover, gout or hyperuricemia is clearly associated with avariety of comorbidities, including cardiovascular diseases, chronic kidney disease, urolithiasis, metabolic syndrome, diabetes mellitus, thyroid dysfunction, and psoriasis.

To prevent acute arthritis attacks and complications,earlier use of pharmacotherapeutic treatment should be considered, and patients with hyperuricemia and previous episodes of acute gouty arthritis should receive long-term urate-lowering treatment.

Urate-lowering drugs should be used during the inter-critical and chronic stages to prevent recurrent gout attacks, which may elicit gradual resolution of tophi.

The goal of urate-lowering therapy should aim to maintain serum uric acid (sUA) level <6.0 mg/dL. For patients with tophi the initial goal can be set at lowering sUA to <5.0 mg/dL to promote tophidissolution.

The goal of this consensus paper was to improve gout and hyperuricemia management at a more comprehensive level. The content of this consensus paper was developed based on local epidemiology and current clinical practice, as well as consensuses from two multidisciplinary meetings and recommendations from Taiwan Guideline for the Management of Gout and Hyperuricemia.

READING 10 – SAFETY OF TREATMENT OPTIONS AVAILABLE FOR GOUT

Schlesinger N. The safety of treatment options available for gout. Expert Opinion onDrug Safety. 2017 Apr; 16(4):429-36.

Doi: 10.1080/14740338.2017.1284199. Epub 2017Jan 30. Review. PubMed
PMID: 28095258 [Payment required]

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ABSTRACT
INTRODUCTION: Gout is the most common inflammatory arthritis in humans. Gout treatment includes rapid initiation of anti-inflammatory medications for acute attacks and chronically treating with urate lowering drugs as well as chronic anti-inflammatory prophylaxis.

Areas covered: This review aims to provide an overview and discussion of the safety concerns of current treatment options available for gout.

Expert opinion: Gout is a curable disease with appropriate treatment. The advent of new therapies provides encouraging opportunities to improve gout management. However, clinicians should be aware of some of the safety concerns of medications used to treat acute and chronic gout. When prescribing medications for gout one has to be mindful of the presence of comorbidities commonly affecting gout patients that may affect drug safety and efficacy, especially in the elderly and in patients treated with multiple drugs. The benefits of gout drugs, usually, outweigh their safety concerns.

Studies are needed in gout patients with chronic kidney disease and/or cardiovascular disease, so that escalation of dosing /combination of anti-inflammatory drugs needed to suppress gouty inflammation as well as escalation of dosing/combination of urate lowering drugs needed to achieve target serum urate level will lead to better understanding of gout treatment safety issues.