THE MALAYSIAN CONSENSUS ON THE MANAGEMENT OF ACUTE & PERSISTENT HYPERKALAEMIA:

A MULTIDISCIPLINARY APPROACH 2024

NATIONAL HEART ASSOCIATION OF MALAYSIA

MALAYSIAN SOCIETY OF NEPHROLOGY

COLLEGE OF EMERGENCY PHYSICIANS ACADEMY OF MEDICINE, MALAYSIA

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SUMMARY

Hyperkalaemia (HyperK^+) is a potentially life-threatening condition that poses significant challenges in both acute and chronic care, especially for patients with chronic kidney disease, heart failure, and diabetes mellitus. While renin-angiotensin-aldosterone system inhibitors (RAASi) are a guideline-directed medical therapy known for their cardiorenal benefits, concerns about the increased risk of hyperK^+ associated with these medications have hindered their optimal use. Despite these challenges, ambiguity remains regarding the management of hyperK^+, highlighting the need for a standardised approach. This Malaysian consensus provides evidence-based guidelines for managing acute and persistent hyperK^+ tailored to the local healthcare context.

A multidisciplinary panel of experts, including nephrologists, cardiologists, and emergency physicians, reviewed current evidence and international guidelines to develop 16 consensus statements. These statements address key areas, which include the definition of hyperK^+, emergency management strategies, long-term treatment with novel potassium binders, and collaborative care practices. The consensus emphasises early identification, individualised care, and the role of novel therapies like sodium zirconium cyclosilicate and patiromer in optimising RAASi therapy.

Through this consensus, the panel aims to improve outcomes for cardiorenal patients by providing a structured approach to managing hyperK^+ in Malaysia.

CONSENSUS STATEMENTS DEVELOPMENT

The development of the consensus statements involved a comprehensive and structured process. A steering committee (SC) comprised of 12 members, including emergency physicians (3), nephrologists (5), and cardiologists (4), was formed to develop these statements.

The initial phase involved a scoping review of recent consensus statements and guidelines followed by the creation of 49 statements across six major themes, which were the definition of hyperK$^+$, diagnosing and managing hyperK$^+$ in emergency settings, preventing hyperK$^+$ in at-risk cardiorenal patients, assessing risk and managing hyperK$^+$ in cardiorenal patients, K$^+$-lowering therapies for hyperK$^+$ in cardiorenal patients, and collaborative care. These statements aimed to recommend diagnosis and treatment approaches for hyperK$^+$ in both acute (emergency) and persistent settings. The initial statements were presented to the SC for extensive discussion. Through this process, the number of statements was reduced to 20, while maintaining the original six themes. The revised 20 statements were then developed into a survey using Microsoft Forms. All submissions were anonymised, and consent was implied when specialists answered the survey on a volunteer basis.

The survey was distributed to all registered specialists through their respective professional societies: the College of Emergency Physicians, the Malaysian Society of Nephrology, and the National Heart Association of Malaysia. Based on the combined number of registered specialists, the SC agreed that a response rate of approximately 30% would be acceptable. The survey duration was set for two months to allow optimal response time.

The statements were evaluated using a 4-point Likert scale, "Strongly agree, Agree, Disagree and Strongly disagree", with an option to provide comments for each statement. Votes of "Strongly agree" and "Agree" were totalled to determine the level of agreement. Statements with ≥75% agreement were included in the consensus.

A total of 169 responses were received from the survey, comprising 24% nephrologists (n=41), 36% cardiologists (n=61), and 40% emergency medicine physicians (n=67).

In terms of years of experience, the majority of nephrologists (61%) and approximately one-third of cardiologists (39%) had >10 years of experience. Conversely, an equal proportion of emergency medicine physicians (31%) had 5-10 years (31%) and >10 years (30%) of experience. Specifically, among nephrologists, 17% had 5-10 years, 15% had 2-<5 years, and 7% had <2 years of experience. For cardiologists, 21% had 5-10 years, 20% had 2-<5 years, and 18% had <2 years of experience. Among emergency medicine physicians, 27% had 2- <5 years, and 12% had <2 years of experience.

The majority of respondents (58%) were from Ministry of Health (MoH) hospitals, followed by 26% from private hospitals and 16% from university hospitals. Among nephrologists, 49% were from MoH hospitals, 34% from private hospitals, and 17% from university hospitals. Cardiologists were evenly split between MoH hospitals (44%) and private hospitals (44%), with a smaller percentage from university hospitals (11%). Most emergency medicine physicians (76%) were from MoH hospitals, with 19% from university hospitals and 4% from private hospitals.

The SC reviewed the votes and comments in detail. All statements achieved a level of agreement of 75% or higher among the participants (Appendix 1). Following the review, the 20 statements were further reduced and refined to 16 final statements (Table 1). The final statements were based on the latest available evidence. In cases where evidence was lacking, or recommendations were not feasible in the Malaysian context, a consensus was reached among the SC members. The finalised statements were designed to provide clear, evidence-based recommendations for managing acute and persistent hyperK$^+$ in the Malaysian healthcare system. In addition, algorithms for managing acute (Figure 1) and persistent (Figure 2) hyperK$^+$ were developed.

TARGET USER

These consensus statements are intended to guide those involved in the management of patients presenting with acute hyperK$^+$, having persistent (chronic) hyperK$^+$ or at risk of hyperK$^+$ in primary, secondary and tertiary healthcare settings in the public and private sectors. It namely targets medical officers, specialists, trainee specialists and medical students.

SOURCE OF FUNDING

The development of these consensus statements was supported by an unrestricted grant from AstraZeneca Malaysia. AstraZeneca Malaysia played no role in the discussions and consensus process.

DECLARATION OF CONFLICT OF INTEREST

Dr. Ching Chen Hua, Dr. Mohd Rahal Bin Yusoff, Dr. Shaik Farid Abdul Wahab, Dr. Azmee bin Mohd Ghazi and Dr. Siti Suhaila Hamzah declare no conflict of interest.

Dr. Lim Soo Kun has received honorarium for presenting lectures and Advisory Boards from Astellas, AstraZeneca, Baxter, Boehringer Ingelheim, Bayer. Duopharma, Fresenius-Kabi, MSD, Novartis, Novo Nordisk, Roche, Sanofi and Taisho.

Dr. Liew Houng Bang has received support for attending meetings and/or travel by AstraZeneca Sdn Bhd.

Dr. Paranthaman Kaneson has received honoraria for presenting lectures from AstraZeneca Sdn Bhd.

Dr. Prasad Menon has received honoraria for presenting lectures from AstraZeneca Sdn Bhd, Viatris and ZP Therapeutics.

Dr. Sunita Bavanandan has received honoraria for presenting lectures from Boehringer Ingelheim, Bayer and AstraZeneca Sdn Bhd. She also holds the following leadership roles: Chair of ISN OSEA Regional Board, Honorary Secretary Asian Pacific Society of Nephrology, Executive Committee Member KDIGO, and a member of the National Kidney Foundation Board of Directors.

Dr. Tan Li Ping has received honorarium for presenting lectures and other education events from Sanofi, Boehringer Ingelheim, Novartis, Novo Nordisk, AstraZeneca, Fresenius, Duopharma and Bayer. He has also received payment for expert testimonies and participated in Advisory Boards for Bayer, Novo Nordisk, Fresenius and Boehringer Ingelheim. Additionally, he holds leadership roles in the Malaysian Society of Nephrology and the National Kidney Foundation. He holds multiple stock or stock options, but not in AstraZeneca.

Dr. David Chew Soon Ping has received honorarium for presenting lectures from Johnson & Johnson and ZP Therapeutics, and participated in an Advisory Board for Otsuka. He was a committee member for the development of the 2023 Malaysian Clinical Practice Guidelines for Heart Failure.

ACKNOWLEDGMENT

The development committee would like to express their gratitude to the College of Emergency Physicians, the Malaysian Society of Nephrologists, and the National Heart Association of Malaysia councils for distributing the survey to their members, and all the respondents for participating in the survey and their comments and feedback on the consensus statements.

TABLE 1. CONSENSUS STATEMENTS ON THE MANAGEMENT OF ACUTE AND PERSISTENT HYPERKALAEMIA

Definition of hyperK⁺
1. The definitions of hyperK⁺ are – mild: K⁺ 5.5-5.9 mmol/L, moderate: K⁺ 6.0-6.4 mmol/L and severe: K⁺ ≥6.5 mmol/L.
Diagnosing and managing hyperK⁺ in emergency settings
2. It is essential to consider the entire clinical picture when diagnosing and treating patients with hyperK⁺ because it can manifest with non-specific symptoms or be asymptomatic.
3. All patients presenting to the ED with serum K⁺>5.5 mmol/L should undergo an ECG.
4. Initiating treatment strategies in the ED is recommended for patients with serum K⁺ >6.0 mmol/L regardless of ECG changes and in all patients with hyperkalaemic ECG changes.
5. Reassess serum K⁺ levels, and monitor ECG, vital signs, and plasma glucose at a frequency appropriate to the clinical context until the serum K⁺ improves to <5.5 mmol/L.
6. Patients who have responded to treatment (i.e., serum K⁺ <5.5 mmol/L), are stable, with no indication for admission or risk of recurrent hyperK⁺ may be discharged with preventive care and a follow-up appointment.
Preventing hyperK⁺ in the at-risk cardiorenal patients
7. Consider preventive strategies for patients at risk of hyperK⁺.
8. Consider using a K⁺ binder for RAASi optimisation in patients with known hyperK⁺ when basic preventive strategies fail.
Assessing risk and managing hyperK⁺ in cardiorenal patients
9. When RAASi are initiated, closer serum K⁺ monitoring is recommended for high-risk patients (patients with CKD, HF, and/or DM).
10. In an individualised care plan, effectively managing hyperK⁺ is recommended to optimise GDMT.
11. In cases of mild and moderate hyperK⁺, consider decreasing the RAASi dosage if mitigation strategies prove ineffective for normalising serum K⁺ levels.
12. In cases of severe hyperK⁺, consider de-escalating or discontinuing RAASi when the risks outweigh the benefits of continuation.

K^+-lowering therapies for hyperK^+ in cardiorenal patients

13. Managing persistent hyperK^+ with long-term use of novel K^+ binders (SZC or patiromer) may enable cardiorenal patients to experience the proven benefits of guideline-recommended doses of RAASi therapy.
14. CPS is an option for short-term hyperK^+ management. Exercise caution when using CPS in the medium or long-term due to concerns about GI side effects.

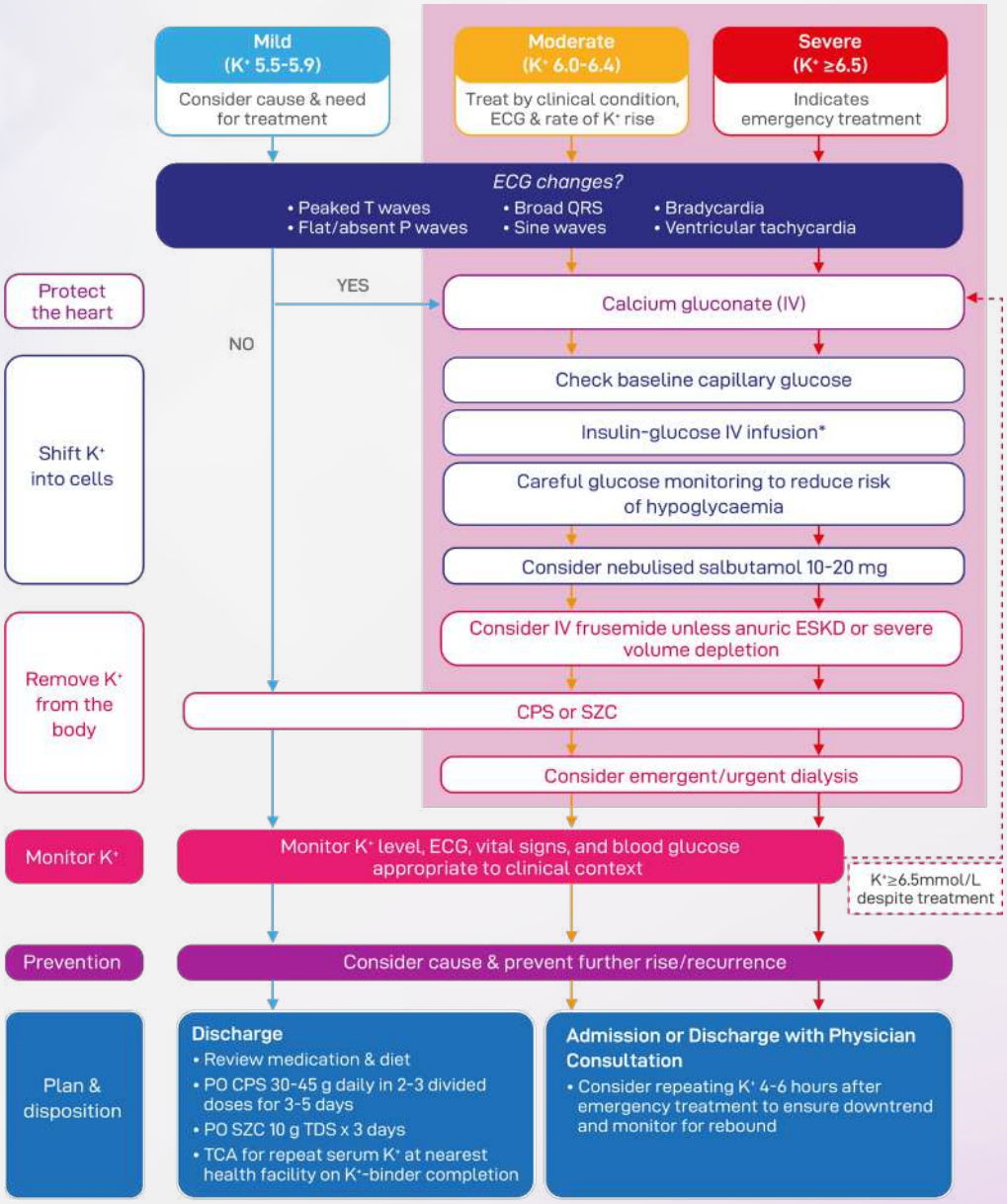
Collaborative care

15. In all cases presenting to the ED with moderate and severe hyperK^+ and are unresponsive to treatment, a physician consultation is recommended.
16. To optimise GDMT, and align medication prescriptions and adjustments relating to hyperK^+, cross-specialty communication is essential.

CKD, chronic kidney disease; CPS, calcium polystyrene sulfonate; DM, diabetes mellitus; ECG, electrocardiogram; ED, emergency department; GDMT, guideline-directed medical treatment; GI, gastrointestinal; HF, heart failure; hyperK^+, hyperkalaemia; K^+, potassium; RAASi, renin-angiotensin-aldosterone system inhibitors; SZC, sodium zirconium cyclosilicate.

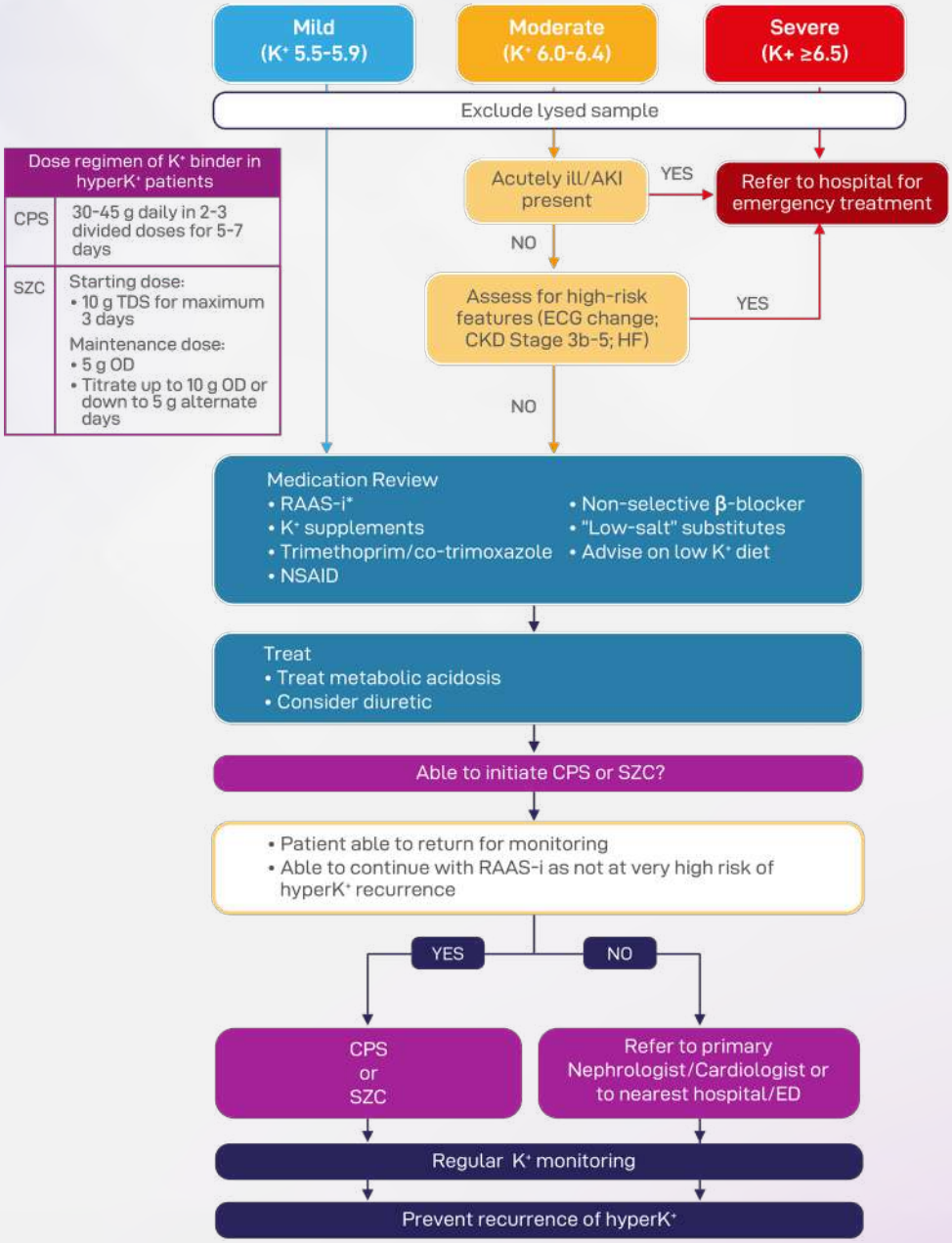
FIGURE 1. EMERGENCY MANAGEMENT OF HYPERKALAEMIA (HYPERK⁺)

- Assess using ABCDE approach
- 12-lead ECG for all patients K^+ ≥5.5 mmol/L (monitor cardiac rhythm if K^+ ≥6.0 mmol/L)
- Exclude lysed sample



*All K^+ levels are in mmol/L. *Give 10 U soluble insulin + 50 ml Dextrose 50% (or equivalent strength) through a slow bolus. ABCDE, Airway, Breathing, Circulation, Disability, Exposure approach; CPS, calcium polystyrene sulfonate; ECG, electrocardiogram; ESKD, end-stage kidney disease; ICU, intensive care unit; IV, intravenous; K^+, potassium; PO, orally; SZC, sodium zirconium cyclosilicate; TCA, to come again; TDS, three times daily. Adapted from The Renal Association UK. Clinical Practice Guidelines. 2020.*[1]

FIGURE 2. MANAGEMENT OF HYPERKALAEMIA (HYPERK⁺) IN THE OUTPATIENT SETTING



*All K⁺ levels are in mmol/L. *RAAS-i = ACE-i/ARB, ARNI and MRA.*

ACE-i, angiotensin-converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin II receptor blocker; ARNI, angiotensin receptor-neprilysin inhibitor; CKD, chronic kidney disease; CPS, calcium polystyrene sulfonate; ECG, electrocardiogram; ED, emergency department; HF, heart failure; K⁺, potassium; MRA, mineralocorticoid receptor antagonist; NSAID, non-steroidal anti-inflammatory drug; PO, orally; TDS, three times daily; RAAS-i, renin-angiotensin-aldosterone system inhibitor; SZC, sodium zirconium cyclosilicate. Adapted from The Renal Association UK. Clinical Practice Guidelines. 2020.[1]

1.0 INTRODUCTION

In healthy individuals, serum potassium (K^+) levels are tightly regulated and maintained between 3.5-5.0 mmol/L through a balance of intake and excretion.[2,3]

- Studies have shown a U-shaped relationship between serum K^+ levels and mortality, with increased mortality observed when K^+ levels deviate from the normal range.[3,4]
- In patients with heart failure (HF), chronic kidney disease (CKD), and diabetes mellitus (DM), a large retrospective study (n=911,698) found that all-cause mortality increases when serum K^+ levels fall outside the 4.0-5.0 mmol/L range.
- The study also observed that mortality rises with each 0.1 mmol/L increment above 5.0 mmol/L.[4]

Patients with **DM, HF,** and particularly **CKD** are at a significantly **higher risk of developing hyperkalaemia (hyperK$^+$)** than the general population.[2,4,5]

- The use of renin-angiotensin-aldosterone system inhibitors (RAASi), comprising of angiotensin-converting enzyme inhibitors/angiotensin II receptor blockers (ACE-i/ARB), angiotensin receptor/neprilysin inhibitors (ARNI), and mineralocorticoid receptor antagonists (MRA), as a component of guidelines-directed medical therapy (GDMT)[6–10] for HF, CKD with proteinuria, and DM with hypertension, further increases this risk.
  - In clinical trials involving renin-angiotensin system (RAS) blockers (ACEi/ARB and MRA), the rates of hyperK$^+$ events were reported to be 5.0% to 20.0%.[11–14]
- Chronic (persistent) hyperK$^+$, defined as a recurrent elevation in serum K^+ above normal limits, can lead to adverse cardiac effects and is common among patients with HF, CKD, and those on RAASi, resulting in medication changes in nearly 50% of affected patients.[15]

Even with the availability of effective novel K^+ binders like patiromer and sodium zirconium cyclosilicate (SZC) for long-term use, and the K^+-lowering resin, calcium polystyrene sulfonate (CPS),[16–18] concerns about the increased risk of hyperK$^+$ due to RAASi in these high-risk populations have hindered the optimisation of RAASi therapy.[11,12,19,20]

- Sub-optimal RAASi dosing occurs although evidence shows that it worsens long-term mortality and hospitalisation rates in HF patients and increases the risk of cardiovascular (CV) events in CKD patients.[11,12,21–26]

Despite this, ambiguity remains about the definition and thresholds of hyperK$^+$ and managing acute and persistent hyperK$^+$ in the cardiorenal population. These consensus statements aim to offer recommendations for managing acute and persistent hyperK$^+$, incorporating the perspectives of emergency physicians, nephrologists, and cardiologists. These recommendations are based on the latest evidence, international guidelines, and best clinical practices within the Malaysian healthcare system.

2.0 CONSENSUS STATEMENTS

1. Definition of hyperK⁺

1.1 The definitions of hyperK⁺ are – mild: K⁺ 5.5-5.9 mmol/L, moderate: K⁺ 6.0-6.4 mmol/L and severe: K⁺ ≥6.5 mmol/L.

The **Kidney Disease: Improving Global Outcomes (KDIGO)** suggests the classification of hyperK⁺ severity should consider complementing the absolute serum K⁺ level with the presence or absence of hyperkalaemic-based electrocardiogram (ECG) changes.[27]

- However, the KDIGO recommendations are specifically for patients with CKD, and these patients have a lower risk of mortality associated with corresponding hyperK⁺ severity than other populations.[28]
    - Patients with no CKD had a significantly higher risk of mortality at serum K⁺ 5.5-5.9 mmol/L (Odds ratio [OR] 10.32) than at serum K⁺ <5.5 mmol/L.
    - The risks tripled (OR 31.64) when serum K⁺ levels were ≥6.0 mmol/L.

Additionally, it is crucial to ensure that the high serum K⁺ levels are not due to **pseudohyperK⁺**.

- PseudohyperK⁺ (factitious, artefactual and spurious hyperK⁺) is a falsely elevated serum K⁺ despite a normal in vivo K⁺ concentration.[29]
- Some causes of pseudohyperK⁺ include:[30]
    - fist clenching during blood draw
    - lysed samples (due to tourniquet time >1 minute, mechanical trauma, using a pneumatic tube without cushioning, use of fine gauge needles, and duration of blood sample storage)
    - thrombocytosis
    - leucocytosis

Therefore, based on the evidence and current best practice, **this consensus guidance defines hyperK⁺** without including ECG changes.

The definitions of hyperK⁺ are:

i. Mild hyperK⁺: serum K⁺ 5.5-5.9 mmol/L
ii. Moderate hyperK⁺: serum K⁺ 6.0-6.4 mmol/L
iii. Severe hyperK⁺: serum K⁺ ≥6.5 mmol/L

2. Diagnosing and managing hyperkalaemia in emergency settings

ECG changes arise when the balance between intracellular and extracellular K^+ is disrupted, typically with serum K^+ >5.5 mmol/L.

- This imbalance increases cell membrane excitability, which can lead to muscle weakness and, in severe cases, cardiac arrest during diastole.[31,32]
- However, while ECG changes are a useful indicator of deviations in serum K^+ levels, **hyperK^+ often presents without noticeable signs and symptoms** and is frequently detected incidentally through laboratory tests conducted for other medical issues.[33]

Life-threatening cardiac dysrhythmias generally occur at serum K^+ levels >6.5 mmol/L, though they can manifest at lower levels in some patients.

- Conversely, those with persistent hyperK^+ may not exhibit ECG changes and can remain asymptomatic even at higher K^+ levels (see **Statement 2.2**).[27,33]
- Additionally, it is important to consider that **symptomatic manifestations of hyperK^+ depend not only on the absolute serum K^+ level but also on the rate at which it increases.**[33]

Assessing hyperK^+ accurately and initiating emergency treatment, especially in the emergency department (ED), is challenging due to uncertainties about the rate of serum K^+ increase and distinguishing acute from persistent hyperK^+.

- Comprehensive patient history and clinical assessment are essential for appropriate treatment.
- ECG changes that could lead to lethal arrhythmias underscore the need for timely management and ongoing reassessment after initiating acute treatment.

Although current hyperK^+ guidelines provide recommendations for monitoring serum K^+ levels,[1,30,34,35] they do not fully address essential parameters such as cardiac monitoring and monitoring for hypoglycaemia. Generally, patients whose serum K^+ declines to ≤5.5 mmol/L may be discharged from the ED.[36]

The algorithm for the emergency management of hyperK^+ is presented in **Figure 1**.

2.1. It is essential to consider the entire clinical picture when diagnosing and treating patients with hyperK⁺ because it can manifest with non-specific symptoms or be asymptomatic.

Practice points:

2.1.1 Assess patients for hyperK⁺ even in the absence of symptoms, as life-threatening cardiac arrhythmias may occur at lower serum K⁺ levels and in patients with persistent hyperK⁺.

2.1.2 Be aware of non-specific hyperkalaemic symptoms for timely diagnosis and management.

Patients with hyperK⁺ may present with non-specific symptoms like:[33,37,38]

- fatigue
- muscle weakness or pain
- paraesthesia
- flaccid paralysis
- depressed deep tendon reflexes
- palpitations
- syncope
- dyspnoea
- vomiting or nausea

When assessing the full clinical presentation, identifying risk factors of hyperK⁺ is essential. These include,

- a history of concurrent comorbidities (CKD, diabetic kidney disease [DKD], HF)
- medication history
- presenting complaints and other investigative findings indicating other causes of acute hyperK⁺, e.g., infections, uncontrolled hyperglycaemia, and acute kidney injury (AKI).

2.2. All patients presenting to the ED with serum K^+ >5.5 mmol/L must undergo an ECG.

Practice points:

2.2.1 Although ECG sensitivity for mild hyperK^+ is low, increased serum K^+ can induce detectable ECG changes.

Changes in the ECG can occur even with mild hyperK^+, such as tall, peaked, narrow-based T waves in the V2-V4 leads and fascicular blocks.[31,32,37]

- Progressively increasing serum K^+ induces further ECG changes such as different types of heart blocks, decreasing P-wave amplitude that can be followed by the disappearance of the P-wave, prolonged QRS complex, ventricular dysrhythmias, "sine waves", and finally asystole, in severe hyperK^+.[31,32,37]

The severity of hyperK^+ and ECG changes can be variable, and the **absence of an ECG abnormality does not negate the presence of hyperK^+**.[32,37] Despite this, assessing ECG is an essential screening tool to assess the severity of hyperK+ rapidly.[39]

2.3. Initiating treatment strategies in the ED is recommended for patients with serum K^+ >6.0 mmol/L regardless of ECG changes and in all patients with hyperkalaemic ECG changes.

Practice points:

2.3.1 Accurately differentiating between acute and persistent hyperK^+ is essential to guide appropriate emergency treatments.

2.3.2. Promptly initiate emergency management strategies for hyperK^+ based on the serum K^+ level to prevent ECG changes and potential lethal arrhythmia.

2.3.3. To manage hyperK^+ in the emergency setting, treat reversible causes, reduce membrane excitability (e.g., with intravenous [IV] calcium gluconate), and start measures for lowering serum K^+.

Managing hyperK^+ in the emergency setting consists of four basic steps that are well-established and widely practiced (Figure 1):[33,34,40-45]

1. Determine and treat any reversible cause of the hyperK^+.
2. Take measures to reduce the cardiac membrane excitability with IV calcium salts, like calcium gluconate.
3. Initiate therapeutic measures to reduce serum K^+ levels rapidly:
   - ⓐ Initial treatment should be with IV 50% dextrose and insulin. This combination is useful for patients with relative contraindications to β-2 agonists and those with severe hyperK^+ (serum K^+ ≥6.0 mmol/L or associated ECG changes).
   - ⓑ Subsequently, salbutamol can be administered by nebuliser or IV route.
   - ⓒ Loop or thiazide diuretics may be considered for non-oliguric and volume-overloaded patients. IV frusemide 40 mg can be given every 12 hours or as a continuous infusion for patients with volume overload and preserved kidney function.[33,34]
   - ⓓ K^+-binders may be considered for patients with renal insufficiency.[33,34] However, SZC cannot be used as a stand-alone therapy in life-threatening acute hyperK^+ and should be used in addition to the standard of care.[46]
   - ⓔ Sodium bicarbonate is useful in patients with severe acidosis.
4. If the serum K^+ remains ≥6.5 mmol/L or pathological ECG changes persist, the renal team should be contacted to arrange for urgent dialysis, as haemodialysis is the definitive measure to reduce serum K^+.

2.4. Reassess serum K^+ levels, and monitor ECG, vital signs, and plasma glucose at a frequency appropriate to the clinical context until the serum K^+ improves to <5.5 mmol/L.

Practice points:

2.4.1 Monitoring ECG continuously at and during emergency management of hyperK^+ is advisable.

2.4.2 Monitor other clinical parameters at appropriate intervals on a case-to-case basis.

2.4.3 Monitor glucose levels at regular intervals if the patient is given insulin during the emergency treatment of hyperK^+.

2.4.4 Monitor serum K^+ levels as early 2-4 hours after initiating K^+-lowering agents and then reassess to determine the frequency of monitoring.

The frequency and duration of monitoring depend on:[30]

- the severity of the hyperK^+ and its manifestation
- the type of K^+ lowering drugs administered
- the likelihood of rebound hyperK^+
- the patient's overall clinical context and response to treatment

Monitoring parameters	Methods
ECG	• Continuous ECG and/or cardiac monitoring is suggested for all patients treated for acute hyperK⁺ with serum K⁺ >6.0 mmol/L.[30]
Other vital signs	• Other vital signs, such as blood pressure and oxygen saturation, should also be monitored.[30]
Hypoglycaemia	• Can occur as early as 30 minutes to up to 3.5 hours[47,48] post-insulin-glucose administration. • May persist up to 6 hours.[1] • Monitor glucose frequently within the first hour, followed by appropriate intervals, depending on the insulin and glucose dose administered, pre-treatment glucose levels[49] and other patient-specific risk factors.[50]
Serum K⁺	K⁺- shifting agents • Structured monitoring is typically aligned with the action times of the K⁺-shifting agents, which begin within 30-60 minutes. • As these medications do not remove K⁺ from circulation, rebound hyperK⁺ can potentially occur after 2-3 hours.[30] • Re-evaluation of serum K⁺ can be performed as early as 2-4 hours after administration of agents like insulin-glucose infusion and salbutamol.

	K⁺-binders
	• Using K⁺ binders may help mitigate the rebound effect, though their onset of action varies,
	  ▸ older binders like CPS can take hours to days to exert their effect,[51]
	  ▸ newer binders like SZC act within an hour and patiromer within 4-7 hours.[52]
	• Serum K⁺ levels can be measured at 1-2 hours post-K⁺ binder administration,[1] followed by regular monitoring at appropriate intervals until the patient is discharged from the ED.

2.5. Patients who have responded to treatment (i.e., serum K^+ <5.5 mmol/L), are stable, with no indication for admission or risk of recurrent hyperK^+ may be discharged with preventive care and a follow-up appointment.

Practice points:

2.5.1 Healthcare providers may discharge patients who have a repeat serum K^+ <5.5 mmol/l, resolved ECG changes, and stable vital parameters, with K^+ binders and close follow-up.

2.5.2 Hemodynamic instability, new or persistent ECG changes, and new onset hyperK^+ require admission.

The recent consensus statement from the American College of Emergency Physicians[35] recommends **admission for further** evaluation for patients who,

- do not achieve haemodynamic stability
- continue developing new ECG abnormalities
- have recalcitrant serum K^+ levels
- have no history of hyperK^+

Consider discharging patients from the ED if they fulfil the following criteria:

1. History of persistent hyperK^+ and the cause for the present acute episode has been resolved.
2. Achieving haemodynamic stability and feeling well.
3. Has easy access and avenues for close follow-up.
4. Agrees to discharge after being counselled about the risks and benefits of discharge.

Before discharge, the physician should:

1. Review the patient's current medications and diet.
2. Advise them to withhold any K^+ supplements and to consume a low K^+ diet.
3. Ensure a K^+ binder has been prescribed with the correct dose and duration.
4. Provide a referral letter to the nearest healthcare facility for a repeat serum K^+ on completion of the K^+ binder.
5. Ensure that the precipitating factor has been identified and managed accordingly.

3. Preventing hyperK⁺ in the at-risk cardiorenal patients

K^+ homeostasis is primarily maintained by the kidneys, which excrete K^+.[53]

- Impairment in this process can lead to hyperK⁺.
- Several medications can disrupt the K^+ balance by either causing a transcellular shift of K^+ or by reducing renal excretion.[54]
- Conditions like CKD, HF, DM and hypertension, especially when treated with RAASi, elevate the risk of persistent hyperK⁺, making patients 2-3 times more likely to develop hyperK⁺.[52,53,55,56]
- Additional risk factors include using other drugs like β-blockers, non-steroid anti-inflammatory drugs (NSAIDs), and trimethoprim/sulfamethoxazole, advanced age, and high K^+ intake.[52,55,57] Hence, preventing hyperK⁺ in these at-risk patients is crucial to optimising guideline-directed medical treatment (GDMT) use for better patient outcomes.

3.1. Consider preventive strategies for patients at risk of hyperK⁺

Practice points:

3.1.1 Consider regular blood monitoring for patients at risk of hyperK+ and introduce preventive strategies when serum K^+ is ≥ 5.0 mmol/L.

3.1.2 RAASi should be carefully dosed, and serum K^+ levels should be monitored closely after initiation and up-titration.

3.1.3 Using diuretics can mitigate hyperK+ in patients with volume overload.

3.1.4 Address modifiable risk factors such as avoiding medications and drug combinations that may cause hyperK⁺, avoiding constipation, and correcting metabolic acidosis.

3.1.5 Dietary modification limiting K^+-rich foods, withdrawing K^+-containing supplements and educating patients about hidden K^+ in processed foods are also preventive strategies.

Prescribe hyperK⁺-inducing drugs with caution – The following drugs should be prescribed with caution for individuals who are at high risk of persistent hyperK⁺.[54]

1. Drugs inhibiting the RAAS: These drugs interfere with K^+ homeostasis, causing a reduction in K^+ excretion, leading to hyperK⁺. They include RAASi, NSAIDs, calcineurin inhibitors (e.g., cyclosporine and tacrolimus), heparin and its derivatives, other aldosterone antagonists, K^+-sparing diuretics, trimethoprim and pentamidine.
2. Medications altering transmembrane K^+ movement: They include amino acids, β-blockers, suxamethonium and mannitol.
3. K^+-containing agents: Like salt substitutes and alternatives, penicillin G and stored blood products.

Diet modification – Guidelines recommend that patients at risk of hyperK⁺ should reduce their K⁺ intake in their daily diet.[1,34,56]

- However, there are practical and psychological barriers to adhering to a low K⁺ diet, and limited evidence of the association between dietary K⁺, serum K⁺, and hyperK⁺.[58]
- The latest National Kidney Foundation's Kidney Disease Outcomes Quality Initiative (KDQI) guidelines[59] recommend other K⁺ lowering strategies to effectively prevent hyperK⁺ and specify that adjusting dietary K⁺ intake for adults with CKD stages 3-5D or post-transplantation may be reasonable.
- KDIGO (2024) guidelines[60] recommend educating patients with CKD about dietary modifications (including K⁺ intake) based on their individual needs, the severity of their CKD and other comorbid conditions.
- Patients with CKD or at risk of hyperK⁺ should also be educated about **sources of hidden K⁺ in processed foods**.[61]
    - K⁺ additives in processed foods are used as preservatives, stabilisers, and in flavouring agents and sweeteners.
    - Examples of processed foods with hidden K⁺ include dried fruits, peanut butter, meat derivatives, tomato-based sauces,[61] sweetened and alcoholic beverages and packaged snacks.

Using diuretics – Diuretics, particularly loop diuretics, enhance K⁺ excretion through urine and are commonly prescribed to prevent an increase of serum K⁺ and control overload simultaneously.[27,56]

- Diuretics should be dosed based on the kidney function because their K⁺ -lowering efficacy reduces as kidney impairment advances.
- However, caution must be used by regularly assessing the patient's kidney function and fluid status, as diuretics may cause AKI and electrolyte imbalance, including hypokalaemia.
- In addition, diuretics might not be ideal for long-term use to control serum K⁺ unless there are other reasons for it, such as extracellular volume overload.[56]

Addressing metabolic acidosis – If there is concurrent metabolic acidosis (HCO_3 <22 mmol/L), oral sodium bicarbonate (3-5 g/day) can be considered.

- However, prolonged use of sodium bicarbonate may increase the sodium load, resulting in volume overload. In this circumstance, sodium bicarbonate should be discontinued.[27,56]

3.2. Consider using a K^+ binder for RAASi optimisation in patients with known hyperK^+ when basic preventive strategies fail.

Practice points:

3.2.1 Use optimal doses of RAASi for managing CKD because it reduces albuminuria, increases the rate of albuminuria normalisation and slows CKD progression.

3.2.2 Optimise RAASi for managing HF as it reduces hospitalisations for HF, CV mortality and all-cause mortality.

3.2.3 Consider initiating K^+ binders to facilitate RAASi optimisation in patients with hyperK^+.

Full-dose irbesartan has been shown to significantly reduce the progression to macroalbuminuria over two years, lowering the incidence from 14.9% to 5.2% while also increasing the regression to normoalbuminuria when compared to placebo.[62]

- Additionally, optimal antiproteinuric doses of benazepril and losartan have been found to reduce the risk of doubling serum creatinine, end-stage kidney disease (ESKD), or death by 51% and 53%, respectively, compared to conventional dosages in non-diabetic CKD patients.[63]
- Higher doses of lisinopril have been demonstrated to reduce all-cause mortality or hospitalisation for HF compared to lower doses.[64]
- Eplerenone has also been shown to reduce CV-related mortality, all-cause mortality, and HF-related hospitalisations.[65]
- Maximally tolerated doses of sacubitril/valsartan have been found to reduce the risk of CV death, first hospitalisation for HF, and all-cause mortality when compared to enalapril.[66]

Novel K^+ binders like SZC and patiromer can help optimise dosing of RAASi in patients at higher risk of hyperkalaemia.

- SZC has been shown to effectively correct and maintain normal serum K^+ levels in patients with hyperkalaemia, with 78% achieving normal levels after a 24-72-hour correction phase.[67]
- Over a 12-month maintenance period, up to three-quarters of patients were able to maintain their RAASi dose.
- Patiromer has been found to lower the risk of hyperK^+ (>5.5 mmol/L) and reduce the need for MRA dose adjustments in patients with HF with reduced ejection fraction and a current history of RAASi-related hyperK^+.[68]

4. Assessing risk and managing hyperkalaemia in cardiorenal patients

A population-based analysis revealed that 28% of CKD and 39% of HF patients experienced at least one episode of hyperK⁺.[56]

- A history of hyperK⁺ episodes increases the likelihood of recurrence, underscoring the importance of ongoing vigilance.[56]
- Since individuals at risk for persistent hyperK⁺ may not exhibit symptoms, regular monitoring is essential for early detection and management.

Before considering dose de-escalation or withdrawal, guidelines from the European Society of Cardiology (ESC),[10] American Heart Association/American College of Cardiology (AHA/ACC),[9] and the KDIGO guidelines[6,8] recommend,

- optimising RAASi to the highest tolerated dose,
- close monitoring for hyperK⁺, and
- addressing hyperK⁺.

The algorithm for managing hyperK⁺ in the outpatient setting (persistent hyperK⁺) is presented in **Figure 2**.

4.1. When RAASi are initiated, closer serum K⁺ monitoring is recommended for high-risk patients (patients with CKD, HF, and/or DM).

Practice points:

4.1.1 RAASi elevates hyperK⁺ risk in patients with comorbidities like CKD, HF, and DM, necessitating closer serum K⁺ monitoring.

Patients with CKD	Have a proportionally increasing risk of developing hyperK⁺ with more advanced levels of kidney impairment.[69]
Patients with DM	Have an increased risk of hyperK⁺ due to the associated hyporeninemic hypoaldosteronism.[13,70]
Patients with HF	Are at risk due to multiple factors, including medications used to manage this condition.[13,70]

These risks are additive; hence, an individual with more than one of these conditions (e.g., CKD with HF) would be at a higher risk of hyperK⁺ than an individual with only one of these conditions.[71] For details on initiating and monitoring RAASi, see **Statements 4.3 and 4.4**.

4.2. In an individualised care plan, effectively managing hyperK⁺ is recommended to optimise GDMT.

Practice points:

4.2.1 Patients with HF on GDMT require regular laboratory monitoring for hyperK⁺ and preventive actions against AKI.

4.2.2 To manage hyperK⁺ effectively without interrupting GDMT, prioritise managing all modifiable risk factors.

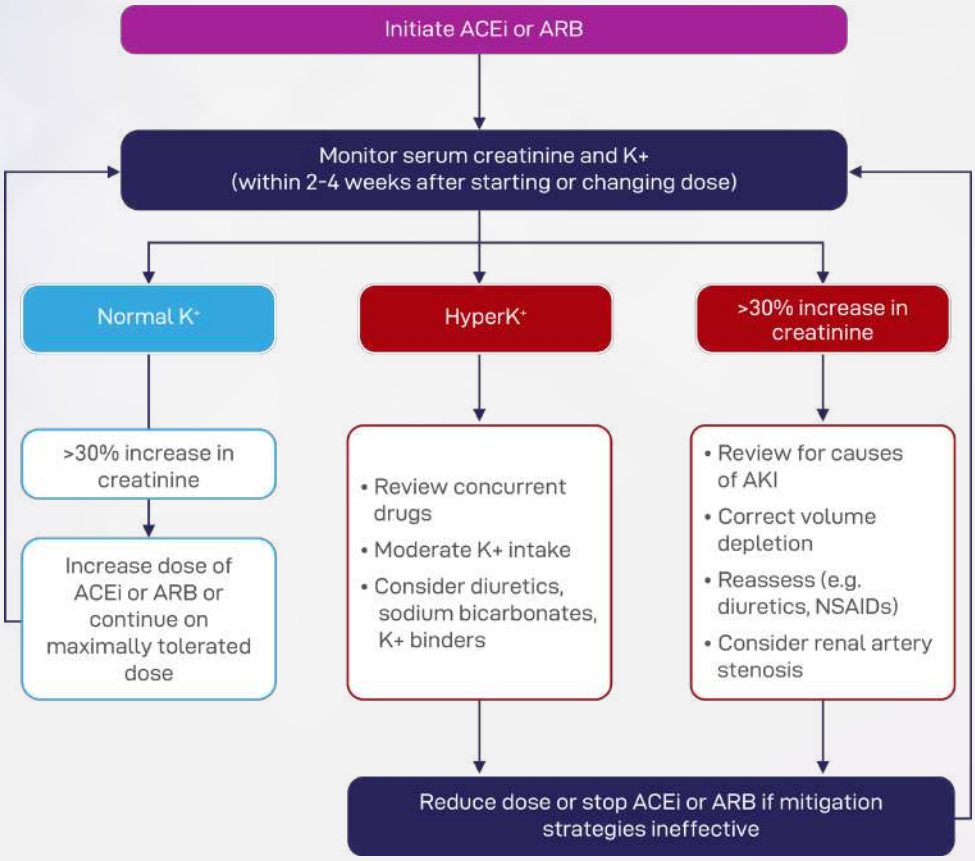
When patients at risk of hyperK⁺ are prescribed GDMTs or other non-disease modifying agents, attention must be given to,

- patient education
- repeat laboratory monitoring
- preventing AKI, which can precipitate hyperK⁺

Shared-decision making is essential in personalising care, and patients should be adequately counselled regarding the risks and benefits of GDMT.[12,22,25]

If hyperK⁺ occurs, effective management involves addressing contributing factors like, diet, use of salt substitutes, acidosis and medications (e.g. K⁺ sparing diuretics and K⁺ supplements) before reducing or discontinuing GDMT.
(**see Statements 3.1-3.3**) **Figure 3** is an example of an individualised care plan to manage hyperK⁺ while optimising GDMT effectively.[6]

FIGURE 3. MONITORING SERUM CREATININE AND K+ DURING ACEI OR ARB TREATMENT WITH DOSE ADJUSTMENT AND MONITORING OF SIDE EFFECTS.



ACE, angiotensin converting enzyme inhibitor; AKI, acute kidney injury; ARB, angiotensin receptor blockers; hyperK+, hyperkalaemia; K+, potassium; NSAIDs, non-steroidal anti-inflammatory drugs. Source: KDIGO 2022 Clinical Practice Guidelines for Diabetes Management in Chronic Kidney Disease.[4] Creative Commons Attribution CC BY-NC-ND-4.0.

4.3. In cases of mild and moderate hyperK⁺, consider decreasing the RAASi dosage if mitigation strategies prove ineffective.

Practice points:

4.3.1 Ensure that all other strategies to mitigate hyperK⁺ have been optimised (see Statements 3.1, 3.2)

4.3.2 Consider a K⁺ binder, if available, to avoid RAASi dose reduction. (see Statements 5.1 and 5.2)

4.3.3 Consider reducing RAASi dose and monitor serum K⁺ level if long-term use of K⁺ binder is not feasible.

4.4. In cases of severe hyperK⁺, consider discontinuing RAASi when the risks outweigh the benefits of continuation.

Practice points:

4.4.1 Ensure all other strategies to mitigate hyperK+ have been optimised (see Statements 3.1, 3.2)

4.4.2 To determine if RAASi can be restarted, temporarily discontinue RAASi and evaluate renal function before deciding on a treatment approach.

4.4.3 Consider a K+ binder, if available, to facilitate reinitiating RAASi. (see Statements 5.1 and 5.2)

The initiation and target doses of RAASi for treating patients with HF can be found within the ESC[10] and AHA/ACC[9] guidelines, while the KDIGO guidelines[6,8] recommend optimising RAASi up to the maximal tolerated dose for managing blood pressure.

- Before considering dose reduction or temporary discontinuation of RAASi, all other strategies to mitigate hyperK⁺, including using oral K⁺ binders, should have been optimised.

Patients with serum K^+ >5.0 mmol/L[72]	• RAASi should be started at a low dose and up-titrated cautiously. • Using novel K^+ binders may be considered to help optimise RAASi utilisation in patients who are either not started on GDMT or have their GDMT not optimised.
Patients with serum K^+ >6.5 mmol/L[72]	• If clinically indicated, RAASi should be temporarily discontinued, and emergency treatment should be initiated to resolve hyperK^+. • Consider novel K^+ binders upon RAASi re-initiation once serum K^+ is normalised to <5.5 mmol/L post-acute treatment.

- Serum K^+ level and kidney function must be evaluated with every dose adjustment made in patients with serum K^+ >5.0 mmol/L.
- Frequency of approaching serum K^+ monitoring has been suggested for ACEi, ARBs and MRAs in Table 3.

Table 3. Frequency of serum K+ monitoring for ACEi, ARB and MRAs.

• At treatment initiation
• 2-4 weeks after initiation but earlier if the patient has kidney impairment with an interval depending on the severity of impairment
• At regular intervals, thereafter, based on the patient's individual risk

5. Potassium lowering therapies for hyperkalaemia in cardiorenal patient

Discontinuation of RAASi treatment following a single hyperK⁺ episode in cardiorenal patients is common despite guidelines recommending continuation.[73]

- Only a small proportion of patients (up to 15%) had RAASi reinstated within six months, with up to 37% having their RAASi dose reduced by more than 25%.[73]
- Reduced RAASi treatment after a hyperK⁺ episode increased all-cause hospital inpatient days by up to 18.2 days within six months.[74]
- It has been reported that hyperK⁺-related RAASi discontinuation or down-titration was associated with a higher risk of cardiorenal events compared to maintained or up-titrated RAASi dosing in patients with CKD or HF.

5.1. Managing persistent hyperK⁺ with long-term use of novel K⁺ binders (SZC or patiromer) may enable cardiorenal patients to experience the proven benefits of guideline-recommended doses of RAASi therapy.

Practice points:

5.1.1 Persistent hyperK⁺ is one of the most important causes of RAASi dosage de-escalation or discontinuation.

5.1.2 Consider using novel K⁺ binders to optimise the use of RAASi as they have demonstrated long-term efficacy and safety.

Novel K⁺ binders (patiromer and SZC) have demonstrated efficacy in reducing serum K⁺ compared to placebo, and safety for long-term use up to 12 months in cardiorenal patients.[16-18]

- This potentially supports GDMT optimisation and reduces the risk of worse outcomes.

  Generally, the trials involving the novel K⁺ binders involved patients with CKD, DM or HF with hyperK⁺.
- The duration of these Phase III trials, including the randomised controlled phase, ranged from 12 days to 27 weeks.
- A few of the studies with an open-labelled maintenance phase ran up to 12 months.[27] The important trials on novel K+ binders, including patiromer and SZC, are summarised in Tables 4 and 5.

Table 4. Patiromer Phase III trials

Trial	Design	Population	Duration	Findings
OPAL-HK[75]	**Multicentre phase 1:** single group, single arm. **Phase 2:** randomised, single-blind, placebo-controlled withdrawal phase.	**Phase 1:** N=243 **Phase 2:** N=107 eGFR <60 (91%), RAASi (100%), DM (57%), HTN (97%), hyperK⁺	**Phase 1:** 4 weeks **Phase 2:** 8 weeks	Mean serum K⁺ reduction in phase 1 was -1.01 mmol/L (p<0.001). Between group difference in serum K⁺ during the withdrawal phase was 0.72 mmol/L (95% CI 0.46–0.99, p<0.001). 60% of the placebo group compared with 15% of the patiromer group had a serum K⁺ reading ≥5.5 mmol/L.
DIAMOND[68]	**Multicentre phase 1:** open label, run in. **Phase 2:** randomised triple-blind placebo-controlled withdrawal phase.	**Phase 1:** N=1195 **Phase 2:** N=878 RAASi (100%), MRA (100%), HTN (91%), HF (100%), hyperK⁺	**Phase 1:** up to 12 weeks **Phase 2:** 13 to 43 weeks (median: 27 weeks)	Serum K⁺ was 0.10 mmol/L higher in the placebo group (p<0.001). Serum K+ >5.5 mmol/L and discontinuation or dose reduction of MRA was less frequent in the patiromer group (HR 0.63 and 0.62, with p=0.006 for both).

CI, confidence interval; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HR, hazard ratio; HTN, hypertension; hyperK⁺, hyperkalaemia; K⁺, potassium; MRA, mineralocorticoid antagonists; RAASi, renin angiotensin-aldosterone system inhibitors.

Table 5. SZC Phase III trials

Trial	Design	Population	Duration	Findings
ZS-003[17]	**Phase 1:** multicentre, double-blind correction phase. **Phase 2:** randomised controlled, multicentre, double-blind maintenance phase.	**Phase 1:** N=753 **Phase 2:** N=543 eGFR <60 (74.5%), RAASi (67%), DM (60%), hyperK⁺	**Phase 1:** 48 hours **Phase 2:** 12 days	In the correction phase, SZC reduced serum K^+ by 0.30% per hour while placebo reduced serum K^+ by 0.09% per hour (p<0.001). During the maintenance phase, SZC 5 g and 10 g significantly decreased mean serum K^+ at days 9 and 15 (5.11 mmol/L vs 4.62 mmol/L and 5.11 mmol/L vs 4.60 mmol/L, respectively; p<0.001 for both) but not at day 21 (5.14 mmol/L vs 4.96 mmol/L, p=0.221). There were no significant between group changes in arrhythmias.
HARMONIZE[76]	**Phase 1:** multicentre, open-label correction phase. **Phase 2:** randomised controlled, multicentre, double-blind maintenance phase.	**Phase 1:** N=251 **Phase 2:** N=237 eGFR ≤60 (69%), RAASi (72%), DM (68%), hyperK⁺	**Phase 1:** 48 hours **Phase 2:** 28 days	By the end of Phase 1, the mean reduction in serum K^+ was - 1.1 mmol/L (p<0.001). In Phase 2, normal serum K^+ levels were obtained more often in the SZC arms (71%, p=0.01; 76%, p=0.002; 85%, p<0.001 for 5 g, 10 g and 15 g, respectively). The differences remained significant in the HF subgroup.

Trial	Design	Population	Duration	Findings
HARMONIZE Open-label extension[18]	Multicentre, open-label, single-arm, maintenance phase extension.	N=121 eGFR ≤60 (74%), RAASi (69%), DM (67%), hyperK⁺	≥11 months	Mean serum K⁺ ≤5.1 mmol/L was achieved by 76.6% to 87.5% of participants, and mean serum K⁺ ≤5.5 mmol/L was obtained by all participants.
ZS-005[67]	**Phase 1:** multicentre, open-label correction phase. **Phase 2:** multicentre, open-label, maintenance phase.	**Phase 1:** N=751 **Phase 2:** N=746 eGFR ≤60 (73%), RAASi (64%), DM (63%), HTN (82%), hyperK⁺	**Phase 1:** 24–72 hours **Phase 2:** up to 12 months	At completion of the correction phase, 78% of the patients had a normal serum K⁺. During the maintenance phase, 74% of participants maintained their RAASi dose.
Kashihara et al.[77]	RCT, multicentre, double-blind (Phase II/III)	N=103 eGFR ≤60 (97%), RAASi (78%), DM (60%),	48 hours	At 48 hours, the proportion of patients with normal serum K⁺ was higher in the SZC 5 g and 10 g arms versus placebo (85.3% and 91.7% vs 15.2%, respectively; p<0.0001).
Kashihara et al.[16]	Multicentre, open-label, single arm correction and maintenance phase.	N=150 eGFR ≤60 (93%), RAASi (71%), DM (58%), hyperK⁺	**Phase 1:** 1–3 days **Phase 2:** 1 year	99% of the patients in the correction phase had normal serum K⁺ after 72 h. ≥65.5% of patients had normokalaemia throughout.

Trial	Design	Population	Duration	Findings
DIALIZE[78]	RCT, multicentre, double-blind.	N=196 mHD (100%), pre-dialysis hyperK⁺	8 weeks	More participants in the SZC arm had pre-dialysis serum K⁺ levels between 4 and 5 mmol/L in at least 3/4 long interdialytic intervals without requiring rescue therapy versus placebo (41.2% vs 1.0%; p<0.001). Rescue therapy for hyperK+ was similar in both arms.
ENERGIZE[46]	RCT, multicentre, double-blind.	N=70 Emergency room, hyperK⁺	10 hours	There was no statistically significant reduction in serum K⁺ between SZC and placebo at 10 hours.

CI, confidence interval; DM, diabetes mellitus; eGFR, estimated glomerular filtration rate; HF, heart failure; HR, hazard ratio; HTN, hypertension; hyperK⁺, hyperkalaemia; K⁺, potassium; mHD, maintenance haemodialysis; MRA, mineralocorticoid antagonists; RAASi, renin-angiotensin-aldosterone system inhibitors; RCT, randomised controlled trial; SZC, sodium zirconium cyclosilicate.

5.2. CPS is an option for short-term hyperK⁺ management. Exercise caution when using CPS in the medium- or long-term due to concerns about gastrointestinal (GI) side effects.

Practice points:

5.2.1 The K+ binder, CPS, is an option for the short-term management of hyperK+.

5.2.2 CPS is administered orally. If the oral route is not feasible or a rapid onset of action is needed, the rectal route can be used.

5.2.3 CPS use in the medium- and long-term should be done with caution as it may cause bowel necrosis, GI intolerance, hypercalcaemia, and hypomagnesemia.

CPS is a K⁺-lowering resin that exchanges calcium for K⁺.

- It acts in the colon and can be administered orally or rectally if the oral route is not an option or rapid onset is needed.[79,80]
- CPS has demonstrated efficacy in reducing serum K⁺ in hyperK⁺ among patients with CKD (Table 5).[79,81,82]
- Even so, an extensive systematic review to determine the efficacy and safety of these resins revealed that there is still a lack of high-quality evidence for using them to treat hyperK⁺.[80]
- The most common and major side effect of CPS is constipation.[83-85]
    - There are some case reports of patients developing intestinal necrosis, resulting from a combined administration of CPS and sorbitol.[83-85]
    - Since there is a small risk of serious intestinal complications, patients prescribed CPS should be closely observed.
    - The product information for CPS recommends that it should be discontinued if there are any abnormal GI side effects, such as severe constipation, prolonged abdominal pain, and vomiting.[79]
    - Data for CPS long-term efficacy is limited. A retrospective study (n=247 with CKD stages 2-5) showed that long-term CPS (mean CPS dose 8.0 ± 3.6 g/day and mean duration 5.6 ± 8.7 months) may be effective and safe for controlling mild hyperK⁺ in patients with CKD.[85]

Table 6. CPS clinical trials

Trial	Design	Population	Duration	Findings
Wang et al., 2018	Prospective, randomised, crossover clinical trial with a 1-week washout period.	58 haemodialysis patients with hyperK⁺ (≥5.5 mol/L).	3-week CPS (3 x 5 g/day) or a blank control, with a 1-week washout period.	Compared with the control group, CPS treatment significantly reduced serum K⁺ levels ($p < 0.01$). More patients in the CPS group had lower serum K⁺ levels than the safety level of <5.5 mmol/L (32% for control vs. 61% for CPS, $p < 0.01$).
Wang et al., 2023	Prospective, open, randomised, controlled, single-centre clinical observational study.	107 stage 3–5 non-dialysis CKD patients with hyperK⁺ group A (15 g/day) or group B (30 g/day).	1 week	After 3 days of treatment, the serum K⁺ levels in groups A and B had decreased by 0.68 ± 0.46 and 0.75 ± 0.43 mmol/L, respectively. After 7 days, the serum K⁺ levels in groups A and B had decreased by 0.64 ± 0.37 and 0.94 ± 0.49mmol/L, respectively.

CKD, chronic kidney disease; CPS, calcium polystyrene sulfonate; K⁺, potassium.

6. Collaborative care

The use of RAASi in managing closely linked diseases requires close cross-speciality treatment approaches to ensure better patient outcomes.[70,86-89]

- The risk of hyperK⁺ with RAASi is less than 2.0% if used as monotherapy, and increases to approximately 5.0% in dual RAASi usage, and up to 10.0% if combined dual therapy is used in patients with HF and CKD.[90]
- It is worth noting that in the real-world setting, the incidence of hyperK⁺ can be as high as 50.0%.[91-94]
- This is most probably due to starting RAASi in unselected or poorly selected patients who did not receive recommended serum K⁺ and kidney function monitoring.[93,94]

6.1. In all cases presenting to the ED with moderate and severe hyperK⁺ and are unresponsive to treatment, a physician consultation is recommended.

Practice points:

6.1.1 Refer patients unresponsive to emergency hyperK⁺ management to nephrologists/physicians.

6.1.2 Ensure referral/follow-up of patients to work up the cause of acute hyperK⁺ and prevent its recurrence.

6.1.3 Refer patients with persistent ECG abnormalities to the relevant specialities.

Patients with moderate and severe hyperK⁺, with or without ECG changes, who do not respond to the initial acute treatment should be referred to the nephrologist for dialysis.

- A K⁺ binder may also be considered a short-term measure to control the serum K⁺ levels.
- These patients should also be referred to a physician to monitor for rebound hyperK⁺ after the initial reduction.
- Further workup is needed to determine the cause of hyperK⁺ and to prevent recurrence.
- A cardiology review is required to ensure cardiac stability if persistent ECG abnormalities are present.[1]

The patient should be monitored in an intensive care setting (e.g. coronary care unit, high dependency unit or the intensive care unit), particularly if they are:

- Anuric with ESKD.
- Severely dehydrated.
- Exhibiting ECG abnormalities with haemodynamic instability.
- Exhibiting an altered conscious level.

6.2. To optimise GDMT, and align medication prescriptions and adjustments relating to hyperK⁺, cross-specialty communication is essential.

Practice points:

6.2.1 Clear channels of communication between cardiology, nephrology, endocrinology, internal medicine, and dietetics is essential to optimise patient care and manage comorbidities associated with hyperK+ and RAAS-i therapy.

Clear communication regarding therapy in patients with HF and CKD should be established. In some cases, close collaboration with dietitians and pharmacists is required to evaluate the patient's diet, use of supplements, salt substitutes and nutraceuticals, and other drugs that can increase the serum K^+. Quality initiative programs should be encouraged to monitor the kidney function and K^+ levels frequently.

CONCLUSION

The effective management of hyperK$^+$ is essential for improving patient outcomes, especially in those with cardiorenal conditions. Optimal management should aim to reduce ED visits and unplanned hospitalisations due to hyperK and its associated complications while allowing optimisation of GDMT. This multidisciplinary set of consensus statements provides comprehensive guidelines based on the latest evidence and beast practices specific to the context of the Malaysian healthcare system.

By standardising the approach to diagnosing and treating both acute and persistent hyperK$^+$, these recommendations aim to **reduce complications, optimise the use of GDMTs like RAASi, and ultimately improve the quality of care for at-risk patients.** The availability of novel potassium binders, such as patiromer and SZC, provides clinicians with effective long-term options that enable the **safe and optimal use of RAASi in high-risk populations.** Through these efforts, healthcare providers can better prevent and manage hyperK$^+$, minimising its impact on patients and the healthcare system.

APPENDIX: AGREEMENT FOR THE 20 CONSENSUS STATEMENTS

Statement	Agreement
1. The definitions of hyperK⁺ are – mild: K⁺ >5.5 mmol/L (5.6-6.0), moderate: K⁺ >6.0 mmol/L (6.1-6.5) and severe: K⁺ >6.5 mmol/L.	93%
2. HyperK+ can manifest with non-specific symptoms or be asymptomatic. Hence, it is essential to consider the entire clinical picture when diagnosing and treating patients with hyperK⁺.	96%
3. Baseline ECG should be done for all patients presenting to the ED with K⁺ >6 mmol/L and is recommended for K⁺ >5.5 mmol/L.	91%
4. Acute treatment strategies should be initiated in patients with K⁺ >6 mmol/L regardless of baseline ECG findings and in all patients with hyperkalaemic-ECG changes with K⁺ >5.5 mmol/L.	90%
5. Reassessment of K⁺ levels, and ECG, vital signs and plasma glucose monitoring are recommended at a frequency appropriate to the clinical context until the K⁺ level is normalised.	96%
6. Post-acute treatment, patients with a normalised K⁺ level who are stable and do not have any other cause for admission or risk of recurrent hyperK⁺ may be discharged with preventive care and follow-up.	92%
7. K⁺-binding agents, loop-diuretics and dialysis are the means to remove K⁺ from the body.	98%
8. Reducing ED visits and unplanned hospitalisations due to complications associated with hyperK⁺ should be a goal of good optimal management.	98%
9. Patients with CKD, HF, and/or DM and patients treated RAASi are at increased risk of hyperK⁺.	97%
10. Effective management of hyperK⁺ should be an integral part of an individualised care plan to optimise GDMT that improves morbidity, mortality and patient outcomes.	97%

Statement	Agreement
11. In mild and moderate hyperK⁺, the de-escalation or discontinuation of GDMTs such as RAASi should only be done as a last resort.	94%
12. In severe hyperK⁺, de-escalation or discontinuation of GDMT can be considered when the risks outweigh the benefits of continuation.	98%
13. For high-risk patients currently not hyperkaliaemic, preventative measures, such as avoidance of certain non-disease modifying agents and foods, should be considered.	98%
14. If basic preventive measures have not been successful, patients with a known history of hyperK⁺ prohibiting the optimisation of RAASi may benefit from using a novel K⁺ binder to facilitate RAASi optimisation.	94%
15. Patients at risk of hyperK⁺ should be monitored closely with a strategy in place to manage K⁺ levels effectively.	97%
16. The long-term use of novel potassium binders (SZC or patiromer) for managing persistent hyperK⁺ may enable guideline-recommended doses of RAASi therapy and allow cardiorenal patients to experience their proven benefits.	98%
17. The use of SPS should be avoided due to concerns about severe GI toxicity, low compliance due to poor palatability.	87%
18. CPS should be used with caution in the medium- or long-term as it may cause GI side effects, including bowel necrosis.	97%
19. Nephrology consultation is recommended for all patients presenting to the ED with moderate and severe hyperK⁺ unresponsive to typical emergency treatment.	94%
20. Cross-speciality communication is essential to align medication prescriptions and adjustments, in addition to optimising GDMTs.	98%

CKD, chronic kidney disease; CPS, calcium polystyrene sulfonate; DM, diabetes mellitus; ECG, electrocardiogram; ED, emergency department; GDMT, guideline-directed medical treatment; GI, gastrointestinal; HF, heart failure; hyperK⁺, hyperkalaemia; K⁺, potassium; RAASi, renin-angiotensin-aldosterone system inhibitors; SPS, sodium polystyrene sulfonate; SZC, sodium zirconium cyclosilicate.

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