Critical Rounds
Vol 4 | Issue 45 | 2023

Critical Rounds Newsletter
VOL 4 | Issue 45 | 2023

Dear Doctor,

Greetings from Micro Labs Limited. We are happy to bring you **"Critical Rounds Newsletter"** which contain latest and interesting news in the field of Critical Care.

This issue contains:

1. Epidemiology of sepsis-associated acute kidney injury in the intensive care unit

2. Assessment of carbapenem-resistant Klebsiella (CRK) isolates against cefiderocol and comparison of cefiderocol susceptibilities using EUCAST and CLSI interpretive criteria

3. Evaluation of the effects of high-dose protein in critically ill patients who developed different Acute kidney injury

4. Case report on pre-excited atrial fibrillation occurred at a relatively late age

Should you require any article or, medical information, please feel free to contact us medicalservices@microlabs.in
free to contact us at medicalservices@microlabs.in
Looking forward to your valuable feedback

Best Regards,
Medical Team, Micro Labs Limited

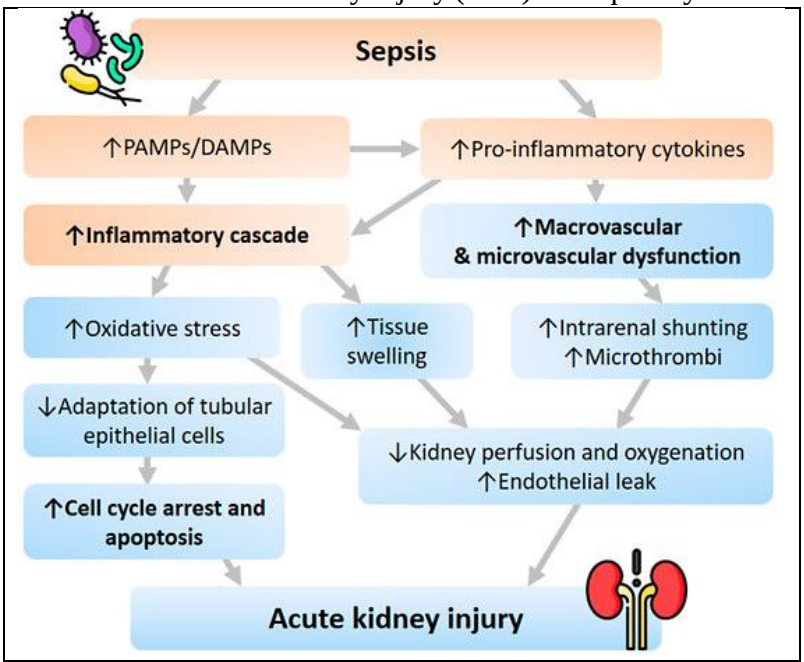
Critical Rounds
Vol 4 | Issue 45 | 2023

Epidemiology of sepsis-associated acute kidney injury in the intensive care unit

Introduction

SA-AKI was prevalent in patients admitted to the ICU from the ED, occurs mostly on the day of ICU admission, and was associated with sepsis and AKI.

Sepsis is a prevalent critical condition that involves immune and blood coagulation system failure, and affected people typically have insufficient tissue perfusion. Several investigations have indicated that individuals with sepsis might have elevated lactate levels due to decreased clearance or liver and renal failure. Hyperlactic acidemia, chronic refractory hypotension, and organ failure following vigorous fluid resuscitation are additional manifestations of sepsis. Studies showed that acute kidney injury (AKI) is frequently caused by sepsis. AKI can occur in as many as 50% of sepsis patients, which was associated with a poor prognosis and a death rate of 75%, which was much greater than that of sepsis patients who do not have organ failure.[1] Recently, the Acute Disease Quality Initiative (ADQI) 28 Workgroup published a definition of sepsis-associated acute kidney injury (SA-AKI). It combines the presence of AKI, as defined by the Kidney Disease Improving Global Outcomes (KDIGO) criteria, occurring within 7 days of the diagnosis of sepsis, with the presence of sepsis, as described by the Sepsis-3 criteria. Based on this standardized consensus definition, the epidemiology of SA-AKI in the severely ill was unclear. Additionally, no research has been done on its occurrence, patient characteristics, trajectory, timing, course of therapy, or outcomes associated with it.[2] So, this study aimed to determine if patients hospitalised to the intensive care unit (ICU) frequently have SA-AKI. This study also performed to test the secondary hypothesis, which states that the majority of SA-AKI was not an intensive care illness, but rather an illness that developed outside of intensive care and lead to admission to intensive care and also investigated the patients with SA-AKI had worse outcomes than non-SA-AKI patients in terms of both renal and non-renal functions.



Sepsis-associated acute kidney injury

Methods

This was a multicentric retrospective cohort study that was conducted in 12 intensive care units (ICUs). The eCritical MetaVision™ clinical information systems were used to gather routinely gathered data from all centres. The author classified patients with proven or suspected infection according on the SEPSIS-3 definition, i.e., patients whose Sequential Organ Failure

Assessment (SOFA) score increased by two points. Using hourly urine output (UO) data and daily serum creatinine, AKI was determined in accordance with the KDIGO definition. Once sepsis and AKI episodes were independently identified, the author used the ADQI 28 Workgroup SA-AKI definition. The day of the AKI diagnosis and the day of the sepsis diagnosis were contrasted. The incidence of SA-AKI was the primary outcome. The timing of SA-AKI in relation to ICU admission, AKI severity, renal recovery status, major adverse kidney events at 30 days (MAKE-30), non-renal, ICU and hospital length of stay, and mortality comprised the secondary outcome.

Results

The SA-AKI criteria were satisfied by 13,451 admissions out of 84,528, with the incidence peaking at 18%. SA-AKI patients were frequently hospitalised from home through emergency department (ED), with a median period from ICU admission to SA-AKI diagnosis of 1 day (interquartile range (IQR) 1-1). The majority of SA-AKI patients (54%) had stage 1 AKI at diagnosis, mostly as a result of the low urine output (UO) criteria alone (65%). Patients identified by UO alone had reduced renal replacement therapy (RRT) needs (2.8% vs 18% vs 50%; $p<0.001$), which was constant throughout all stages of AKI, compared to patients diagnosed by creatinine alone or by both UO and creatinine criteria (figure 1). Hospital mortality from SA-AKI was 18%, and SA-AKI was independently related with higher mortality. In SA-AKI, low UO alone had an odds ratio of 0.34 (95% confidence interval (CI) 0.32-0.36) for mortality compared to creatinine alone or both UO and creatinine criteria.

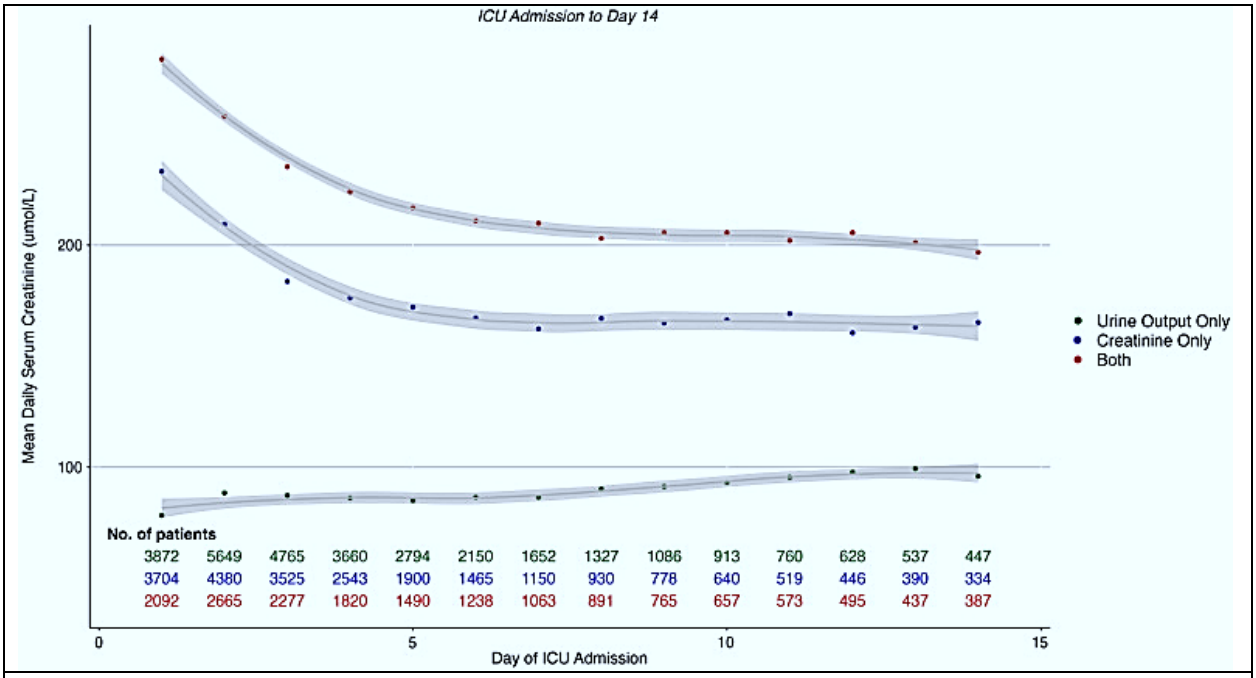


Figure 1. Mean Daily serum creatinine by AKI diagnostic criteria

Discussion

This multicentre study studies over 90,000 critically ill patients and found that SA-AKI occurred in one-sixth of all ICU admissions, that four out of ten such patients were emergency admissions from the community, and that one in four were from hospital ward admissions.

Patients with SA-AKI had more severe illness and needed more organ support treatments as compared to other ICU admissions. The SA-AKI criteria were satisfied by 13,451 admissions out of 84,528, with the incidence peaking at 18%.[2] In the previous single-centre retrospective analysis by Katayama S et al. included only 351 SA-AKI patients and found a relatively low incidence of SA-AKI of 2.8%.[3]

Conclusion

SA-AKI was prevalent in patients admitted to the ICU from the ED, occurs mostly on the day of ICU admission, and is associated with sepsis and AKI. However, most SA-AKI was stage 1 and was caused by low UO, which has a significantly lower risk than other criteria.

References

1. Wang Z, Zhang L, Xu F, Han D, Lyu J. The association between continuous renal replacement therapy as treatment for sepsis-associated acute kidney injury and trend of lactate trajectory as risk factor of 28-day mortality in intensive care units. BMC Emerg Med. 2022 Feb 28;22(1):32.
2. White KC, Serpa-Neto A, Hurford R, Clement P, et al; Queensland Critical Care Research Network (QCCRN). Sepsis-associated acute kidney injury in the intensive care unit: incidence, patient characteristics, timing, trajectory, treatment, and associated outcomes. A multicenter, observational study. Intensive Care Med. 2023 Sep;49(9):1079-1089.
3. Katayama S, Nunomiya S, Koyama K, Wada M, et al. Markers of acute kidney injury in patients with sepsis: the role of soluble thrombomodulin. Crit Care. 2017 Aug 25;21(1):229.

Critical Rounds
Vol 4 | Issue 45 | 2023

Assessment of carbapenem-resistant Klebsiella (CRK) isolates against cefiderocol and comparison of cefiderocol susceptibilities using EUCAST and CLSI interpretive criteria

Introduction

According to EUCAST standards, there was a substantial amount of cefiderocol resistance among NDM producers. This study recommended adopting EUCAST interpretation criteria for cefiderocol susceptibility testing until further clinical outcome data were available.

Infections caused by carbapenem-resistant Klebsiella (CRK) are associated with considerable morbidity and mortality in hospitalised patients.[1] Due to the present restricted treatment choices for multidrug-resistant (MDR) pathogen-caused illnesses and drug resistance in "cunning bacteria," novel therapeutic approaches are of great importance and urgently required.[2] A novel cephalosporin, Cefiderocol has in vitro action against metallo-beta-lactamase as well as all other clinically significant carbapenemases. Treating patients effectively requires reliable antimicrobial susceptibility testing (AST). Because broth microdilution (BMD) requires iron-depleted medium, Cefiderocol AST is still difficult to use. Another difficult aspect of cefiderocol AST is the significant disparity in interpretative criteria between EUCAST and CLSI.[1] The purpose of this investigation was to compare cefiderocol susceptibilities using European Committee for Antimicrobial Susceptibility Testing (EUCAST) and Clinical and Laboratory Standards Institute (CLSI) interpretation criteria, and to illustrate the differences that might result from variations at the breakpoint.

Methods

This was a multicentre observational study. The detection of carbapenem resistance was done by automated methods at participating laboratories and was verified with Etest. A unique collection (n = 254) of mostly OXA-48-like or NDM-producing CRK bloodstream isolates were evaluated using disc diffusion (Mast Diagnostics, UK) against cefiderocol. Bioinformatics analysis on whole bacterial genomes were used to identify beta-lactam resistance genes and multilocus sequence types. The results were evaluated using EUCAST and CLSI breakpoints.

Results

A total of 254 isolates of Klebsiella spp were included (92% Klebsiella pneumoniae, 6% Klebsiella variicola, 0.4% Klebsiella quasipneumoniae and 0.4% Klebsiella oxytoca). In the central laboratory, fifty (20%) of the isolates were determined to be susceptible to carbapenem and did not harbour any carbapenemases. The median cefiderocol inhibition zone diameter for all isolates was 24 mm (interquartile range [IQR] 24-26 mm) and 18 mm (IQR 15-21 mm) for NDM producers (Figure 1). Cefiderocol susceptibilities were shown

to vary significantly between EUCAST and CLSI breakpoints in this investigation. According to these interpretative criteria, 26% and 2% of all isolates and 81% and 12% of NDM producers, were resistant to cefiderocol, respectively.

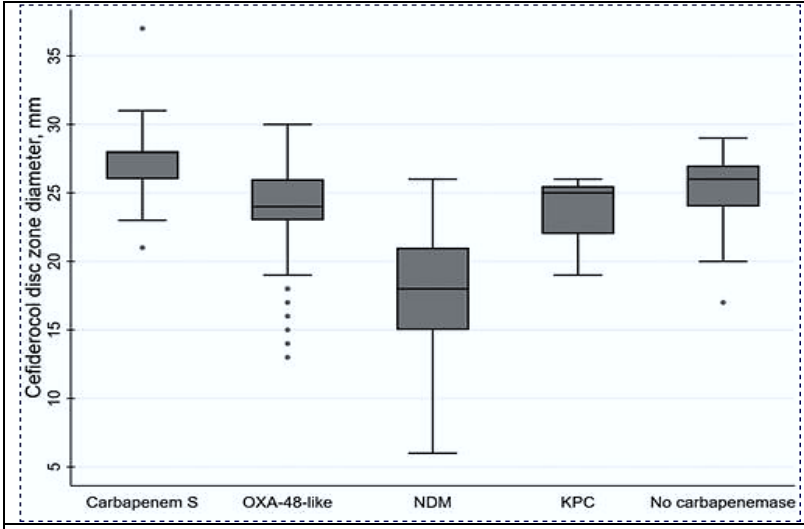


Figure 1. Box plot graph of zone of cefiderocol inhibition diameter as per carbapenem resistance mechanism. S: susceptible.

Discussion

Using EUCAST vs. CLSI breakpoints, there was a notable difference in resistance rates, especially for metallo-beta-lactamase producers, with the former having substantially greater resistance rates.[1] In vitro surveillance studies have previously shown elevated cefiderocol MICs for NDM producers, and co-presence of an ESBL, namely CTX-M, was shown to be more common among cefiderocol-resistant metallo-beta-lactamase producers.[3] In the present study, cefiderocol-resistant metallo-beta-lactamases were more likely to coexist with an ESBL, especially SHV (sulf-hydryl variable).[1]

Conclusion

NDM producers exhibited significant rates of cefiderocol resistance according to EUCAST recommendations. Patient outcomes might be significantly impacted by breakpoint variability. This study suggested utilising EUCAST interpretation criteria for cefiderocol susceptibility testing until further clinical outcome data were available.

References

1. Isler B, Vatansever C, Özer B, Çınar G, et al. Higher rates of cefiderocol resistance among NDM producing Klebsiella bloodstream isolates applying EUCAST over CLSI breakpoints. Infect Dis (Lond). 2023 Sep;55(9):607-613.
2. Yao J, Wang J, Chen M, Cai Y. Cefiderocol: An overview of its in-vitro and in-vivo activity and underlying resistant mechanisms. Frontiers in medicine. 2021 Dec 7;8:741940.
3. Kohira N, Hackel MA, Ishioka Y, Kuroiwa M, et al. Reduced susceptibility mechanism to cefiderocol, a siderophore cephalosporin, among clinical isolates from a global surveillance programme (SIDERO-WT-2014). J Glob Antimicrob Resist. 2020 Sep;22:738-741.

Critical Rounds
Vol 4 | Issue 45 | 2023

Evaluation of the effects of high-dose protein in critically ill patients who developed different Acute kidney injury

Introduction

To avoid possible harmful consequences, especially in patients who did not have KRT, a recommendation for a higher protein dosage in AKI patients should be carefully reconsidered.

Acute kidney injury (AKI) is a usual complication of critical illness. The maintenance of acid-base balance and subsequent metabolic acidosis are among the homeostatic processes that are impaired by AKI. This leads to an increase in proteolysis and protein catabolism as well as a reduction in transcellular amino acid transport. The utilisation and conversion of amino acids is restricted by this decrease of renal metabolic activity. The use of kidney replacement therapy (KRT) exacerbates amino acid loss in patients with severe acute kidney injury (AKI).[1] Supplemental protein and amino acid delivery from outside sources can help critically ill patients recover by reducing protein loss. Unfortunately, the ideal protein dose for critically sick patients was unclear, and nutrition associations throughout the world provide different recommendations (1.2 to 2.5 g/kg body weight) based on weak data, implying clinical standards for protein dose in critically ill patients. There have been conflicting findings from earlier systematic reviews and meta-analyses of the ideal protein dosage in critical illness.[2] The purpose of this study was to assess the impact of high-dose protein in patients who were in critical condition and were experiencing different stages of AKI.

Methods

An exploratory secondary analysis was carried out by the author on the EFFORT Protein study, which was a pragmatic, worldwide, prospective, investigator-initiated, registry-based, randomized, single-blinded trial that involved 85 Intensive Care Units (ICUs) dispersed across 15 countries. This secondary analysis's primary objective was to determine how protein dosage affected TTDA in AKI patients. Patients who died within 60 days after being admitted to the intensive care unit were deemed to have never been discharged from the hospital alive, regardless of their previous discharge status. The duration of KRT following randomization, the incidence of KRT after randomization, and the 60-day mortality were secondary outcomes. The author also contrasted the urea levels in each group during the course of the first 12 study days. Clinical outcomes were evaluated during the patient's hospital stay, up to a maximum of 60 days after randomization. The assessment of protein and energy delivery was conducted during the initial 28 and 12 days after randomization, respectively.

Results

Of the 1329 randomised individuals, 312 experienced AKI and were included in this study (163 in the high protein dosage group and 149 in the regular protein dose group). In comparison to patients receiving a regular protein dosage, individuals with AKI who

received a high protein dose had higher average levels of urea (19.7±9.8 vs. 17.6±9.7; p=0.04). This difference persisted even after KRT (Table 1). A greater relative risk of 1.4 (95% CI 1.1–1.8) for 60-day mortality and a shorter time-to-discharge alive from the hospital (TTDA) (hazard ratio 0.5, 95% CI 0.4–0.8) were linked to increased protein intake. No subgroup showed a beneficial effect of greater protein, and effect modification was not statistically significant for any of them. However, patients receiving kidney replacement treatment (KRT) seemed to be immune to the adverse effects of higher protein targets. Protein dosage did not significantly correlate with the frequency of AKI, KRT, or KRT duration.

Table 1. Incidence and duration of new kidney replacement therapy and urea levels

W	**AKI patients** (***n*** **= 312)**	**High protein** (***n*** **= 163)**	**Usual protein** (***n*** **= 149)**	***p*** **values**
Duration of kidney replacement from randomization (among patients who received dialysis) * Median [IQR]	(107) 6.0 [3.0–10.0]	(60) 5.0 [2.0–10.0]	(47) 6.0 [4.0–10.0]	0.21
New KRT after randomization	64 (20.5%)	34 (20.9%)	30 (20.1%)	0.87
Average Urea (all patients) (mmol/L)	18.7 ± 9.8	19.7 ± 9.8	17.6 ± 9.7	0.04
Average urea ≥ 30 mmol/L (all patients)	42 (13.5%)	26 (16.0%)	16 (10.9%)	0.18

KRT, Kidney replacement therapy *The duration of KRT from randomization includes 64 incident and 43 prevalent cases of KRT

Discussion

In the present study, regardless of the stage of AKI, a larger protein dosage relative to standard dose in patients with AKI was linked to slower TTDA and higher 60-day mortality. Although the interaction was not statistically significant, it was interesting to note that this damage did not persist in patients who had KRT. High-dose protein did not correlate with increased incidence or longer duration of KRT. The current study findings were the largest to date, demonstrating that greater protein dosage, relative to standard dose, in critically ill patients with AKI was linked with delayed TTDA and increased mortality.[1] It was significant to note that the current results were consistent with Zhu R et al. which showed that extra amino acid delivery negatively affected individuals with acute renal damage.[3]

Conclusion

High protein may be linked to poorer outcomes in all AKI stages in critically ill AKI patients. To prevent potential adverse effects, especially in patients who were not treated with KRT, the recommendation of greater protein dose in AKI patients should be carefully revaluated.

References

1. Stoppe C, Patel JJ, Zarbock A, Lee ZY, et al. The impact of higher protein dosing on outcomes in critically ill patients with acute kidney injury: a post hoc analysis of the EFFORT protein trial. Critical Care. 2023 Oct 18;27(1):399.
2. Lee ZY, Yap CS, Hasan MS, Engkasan JP, et al. The effect of higher versus lower protein delivery in critically ill patients: a systematic review and meta-analysis of randomized controlled trials. Critical Care. 2021 Dec;25(1):1-5.
3. Zhu R, Allingstrup MJ, Perner A, Doig GS. The effect of IV amino acid supplementation on mortality in ICU patients may be dependent on kidney function: Post hoc subgroup analyses of a multicenter randomized trial. Crit Care Med. 2018;46(8):1293–301.

Critical Rounds
Vol 4 | Issue 45 | 2023

Case report on pre-excited atrial fibrillation occurred at a relatively late age

Introduction

Pre-excited atrial fibrillation (AF) is a rare condition that might be the only and predominant manifestation of Wolf-Parkinson-White (WPW) syndrome.

Wolff-Parkinson-White (WPW) syndrome is a prevalent cause of paroxysmal supraventricular tachycardia (PSVT), with a reported frequency in the general population of 0.1 to 0.3%.[1] Louis Wolf, Sir John Parkinson, and Paul Dudley White first documented 11 individuals who had palpitations and a sinus rhythm with a short PR and a delta wave on the ECG. This phenomenon became known as the Wolff-Parkinson-White (WPW).[2] It is characterised by the existence of an extra channel that bypasses the atrioventricular node and induces premature ventricular excitement, running between the atria and the ventricles.[1] Although orthodromic or antidromic reciprocal tachycardia is the most prevalent presentation for individuals with accessory pathways, atrial fibrillation (AF) is also seen in one-third of patients with WPW syndrome.[2] This case report described the case of 72-year-old patient who was admitted to the hospital's emergency department due to sudden onset palpitations during rest.

Case Presentation

This is a case report of a 72-year-old patient who was admitted to the hospital's emergency department due to sudden onset palpitations during rest. He had previously experienced hemorrhagic rectocolitis when he was on sulfasalazine. In addition, his paucisymptomatic atrial hyperexcitability was monitored. His Glasgow Coma Scale score was 13/15. The patient's blood pressure was 80/60 mmHg, heart rate was 200 beats per minute, and there was coldness on his extremities. These all indicated hemodynamic instability. The ECG showed wildly irregular wide-complex tachycardia that was morphologically shifting from one complex to another without a significant alteration in the electrical axis. This resulted in an accordion-like look that was indicative of pre-excited atrial fibrillation (Figure 1).

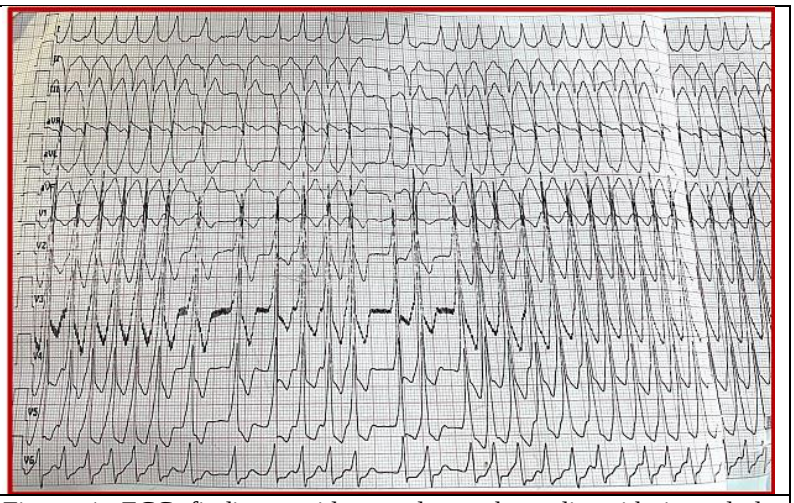


Figure 1. ECG findings: wide-complex tachycardia with irregularly irregular morphology that shifts from one complex to another without significant alteration in the electrical axis, giving the impression of an accordion and suggesting pre-excited atrial fibrillation.

Critical Rounds
Vol 4 | Issue 45 | 2023

The pre-excited RR interval was the shortest at 240 ms, suggesting a risk of ventricular fibrillation degeneration. The patient's unstable neurological and hemodynamic state required the use of an immediate 200 J external electric shock, which resolved the tachycardia and restored the sinus rhythm. With a short PR interval, positive delta wave in V1, negative in the inferior leads, and a V1/DI ratio <1, the ECG in sinus rhythm suggested the presence of a left posteroseptal Kent bundle (Figure 2). The biochemical work-up and the clinical examination were unremarkable. Upon examination of his ECG and Holter ECG, which had been done two years before, no indication of preexcitation was observed. A transthoracic echocardiography (TTE) revealed a bi-atrial enlargement along with normal left ventricular function. With Flecainide and low-dose beta blockers, the patient returned home 5 days later with a favourable outcome.

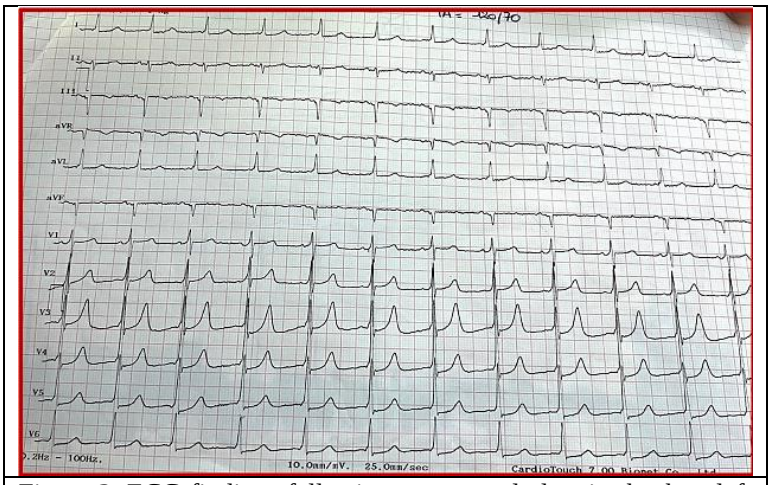


Figure 2. ECG findings following an external electric shock: a left posteroseptal Kent bundle is suggested by the sinus rhythm, short PR interval, positive delta wave in V1, negative in inferior leads, and V1/DI ratio<1.

Discussion

Wolff-Parkinson-White syndrome is distinguished by the presence of one or more atrioventricular accessory pathways that connect the atria and ventricles directly and bypass the AV node, followed by predisposing patients to experience recurrent tachyarrhythmias associated with pre-excitation. The clinical presentation determines how individuals with WPW syndrome and AF are managed. Electrical cardioversion using an external electric shock is most typically utilised in patients with hemodynamic instability. Antiarrhythmic medicines of class IA, IC, or III may be utilised in hemodynamically stable patients. But, all medicines that cause slow AV conduction, include beta-blockers, adenosine, and digitalis, should be avoided.[2] In another case of a 17-year-old female diagnosed with an intermittent preexcitation variant of WPW syndrome was managed with oral atenolol 25 milligrammes twice daily in combination with short-term pediatric cardiology clinic follow-up. It is not recommended to use AV nodal blocking medications such as adenosine or verapamil during AF in WPW.[3]

Conclusion

WPW syndrome is an uncommon condition that can result in sudden death, particularly when associated with atrial fibrillation. As a result, cardiologists must evaluate this diagnosis in individuals who exhibit clinical indications of arrhythmia and an electrical pattern of WPW.

References

1. Coban-Akdemir ZH, Charng WL, Azamian M, Paine IS, Punetha J, et al. Wolff-Parkinson-White syndrome: De novo variants and evidence for mutational burden in genes associated with atrial fibrillation. Am J Med Genet A. 2020 Jun;182(6):1387-1399.
2. Diallo TH, Faraj R, Hilal S, Lahraoui M, Kisra O, Benmessaoud FA, Doghmi N, Fellat I, Cherti M. Pre-excited atrial fibrillation revealed at a very delayed age: case report. International Journal of Emergency Medicine. 2023 Dec;16(1):1-6.
3. Larson NP, Rosenthal JB, Bridwell RE, et al. Hide and Seek: Intermittent Preexcitation Wolff-Parkinson-White Syndrome Case Report and Management Overview. Cureus. 2020 Jul 2;12(7):e8971.

This scientific input is prepared from the Department of Medical Services, an initiative of M/s Micro Labs Limited under the aegis of Micro Knowledge Academy. The information contained herein is for education purpose only. The content is developed by compiling information from various authentic and published literatures. Although great care has been taken to assure the accuracy of the publication, M/s Micro Labs Limited shall not be responsible or in any way liable for any inaccuracy, errors, or omissions resulting from negligence or otherwise howsoever or any consequences arising there from. In spite of best efforts, the information in this publication may become outdated over time. M/s Micro Labs Limited shall not be responsible in any manner whatsoever, for any action taken, opinions expressed, advice rendered or accepted, any direct, incidental, special or consequential loss and damage caused on the basis of any material or information presented in this publication / update.