ansn clinic

腎友週報

安慎、中慎、惠慎
竹東、安新、怡仁

第 288 期
108 / 08 / 28

醫療新知

心房顫動(af)病人接受經皮冠狀動脈介入性治療(PCI)後的藥物治療

----應用在慢性腎臟病或透析病人的考量

- 關鍵字：傳統口服抗凝血劑(VKA, Warfarin)，新一代的口服抗凝血劑(NOAC, non-VKA oral anti-coagulant 或稱 DOAC, direct oral anti-coagulant)，P2Y12 抑制劑(目前台灣臨床上常用 Clopidogrel 與 Ticagrelor)，雙重抗血小板藥物(Dual Antiplatelet Therapy，DAPT，併用阿司匹靈(aspirin)與一種 P2Y12 抑制劑)
- 2019/6/19 JAMA Cardiology 刊出一篇包含 4 個大型隨機對照試驗(randomized controlled trial, RCT)總病人數達 10026 人的統合分析報告，探討心房顫動(af, atrial fibrillation)併冠狀動脈疾病病人因急性冠心症或接受經皮冠狀動脈介入性治療(PCI，即常聽到的氣球擴張術(PTCA)以及支架置放術(Stent)等處置)後較適當的藥物治療選擇。該報告結論：相較於使用傳統口服抗凝血劑(VKA, Warfarin)加上雙重抗血小板藥物(Dual Antiplatelet

Therapy，DAPT)的用藥組合，使用 NOAC 加上 P2Y12 抑制劑併發出血的風險明顯減少。這種不包含阿司匹靈(aspirin)的 NOAC + P2Y12 抑制劑的組合不但比包含阿司匹靈的組合(即 VKA + DAPT 或 NOAC + DAPT)有較低的出血風險，也同樣能達到降低主要心血管不良事件(major adverse cardiovascular events (MACE))的治療效果，並且主張應該避免使用 VKA + DAPT 這類藥物組合。

- 慢性腎臟病(CKD)病人併發出血、血栓栓塞、心血管合併症、心房顫動的風險較常人來得高，而且風險隨著腎功能衰退而上升，特別是透析患者，因此當考慮用抗凝血劑或抗血小板藥物來治療和預防血栓栓塞時，藥物療效與伴隨的出血風險兩者必須權衡。林世杰醫師曾分別在腎友週報 197 期及 274 期介紹『心房顫動的腎友適合使用口服抗凝血劑(Warfarin)預防中風嗎？』及『新一代口服抗凝血劑 DOAC』，點出(1)若沒有絕對必需使用傳統口服抗凝血劑(VKA, Warfarin)的條件，則不建議透析患者使用此藥，(2)對透析患者而言，新一代的 4 種口服抗凝血劑(DOAC)當中，Apixaban **也許是一個比較好的選擇**。
- 不同於歐洲與加拿大，美國 FDA 核准 Apixaban 用於 CKD 第 5 期及透析病人(見下圖，出自 AJKD November 2018)，雖然台灣尚未與美國 FDA 同步，鑑於上述統合分析報告認為不包含阿司匹靈的 NOAC + P2Y12 抑制劑的藥物組合比包含阿司匹靈的藥物組合(即 VKA + DAPT 或 NOAC + DAPT)具有較低的出血風險及相同的治療效果，所以若患有心房顫動的 CKD 或透析病人因急性冠心症必須接受經皮冠狀動脈介入性治療時，Apixaban + P2Y12 抑制劑應該是較好的治療選擇。

Table 2. Dosing Recommendations for NOACs by International Regulatory Bodies in Nonvalvular Atrial Fibrillation for Patients with $eCL_{cr} \leq 30$ mL/min

	Dabigatran	Rivaroxaban	Apixaban	Edoxaban[a]
eCL_{cr} 15-30 mL/min				
FDA	75 mg, 2×/d	15 mg, 1×/d	Standard dosing[b]	30 mg, 1×/d
EMA	Contraindicated	Use with caution (limited clinical data)	2.5 mg, 2×/d	30 mg, 1×/d
Health Canada	Contraindicated	Not recommended	Not specifically addressed	Not recommended
eCL_{cr} < 15 mL/min				
FDA	Dosing recommendations cannot be provided	Not specifically addressed	Standard dosing[b]	Not recommended
EMA	Contraindicated	Not recommended	Not recommended (no clinical experience)	Not recommended
Health Canada	Contraindicated	Not recommended	Not recommended	Not recommended
CKD-5D				
FDA	Dosing recommendations cannot be provided	No specific clinical guidance provided[c]	Standard dosing[b]	Not recommended if eCL_{cr} < 15 mL/min
EMA	Not specifically addressed	Not recommended if eCL_{cr} < 15 mL/min	Not recommended (no clinical experience)	Not recommended
Health Canada	Contraindicated if eCL_{cr} < 30 mL/min	Not specifically addressed	Not recommended	Not recommended

Note: The doses in this table do not account for dosing adjustments (or contraindications) recommended for drug interactions because these vary by regulatory body.
Abbreviations: ARISTOTLE, Apixaban for Reduction in Stroke and Other Thromboembolic Events in Atrial Fibrillation; CKD, chronic kidney disease; eCL_{cr}, estimated creatinine clearance (calculated using Cockcroft-Gault formula); EMA, European Medicine Agency; ESRD, end-stage renal disease; FDA, US Food and Drug Administration; NOACs, non–vitamin K–dependent oral anticoagulants; ROCKET AF, Rivaroxaban Once Daily Oral Direct Factor Xa Inhibition Compared With Vitamin K Antagonism for Prevention of Stroke and Embolism Trial in Atrial Fibrillation.

[a]Post hoc analysis showed a trend toward lower efficacy in reducing the efficacy end point among patients with $eCL_{cr} > 95$ mL/min; thus, edoxaban use is not recommended in this subgroup.

[b]Standard apixaban dosing: 5 mg, twice daily, but reduce dose to 2.5 mg, twice daily if serum creatinine ≥1.5 mg/dL, age 80 years or older, or weight ≤ 60 kg. FDA label states "In patients with ESRD maintained on intermittent hemodialysis, administration of apixaban at the usually recommended dose will result in concentrations and pharmacodynamic activity similar to those observed in the ARISTOTLE study. It is not known whether these concentrations will lead to similar stroke reduction and bleeding risk in patients with ESRD on dialysis as was seen in ARISTOTLE."

[c]FDA label 2017 states: "In patients with ESRD maintained on intermittent hemodialysis, administration of Rivaroxaban 15 mg once daily will result in concentrations and pharmacodynamic activity similar to those observed in the ROCKET AF study. It is not known whether these concentrations will lead to similar stroke reduction and bleeding risk in patients with ESRD on dialysis as was seen in ROCKET AF."

資料來源：中慎診所洗腎室　吳宗翰醫師