５．AHA/ACC Pooled Cohort Equation への腎機能の組み込み “CKD Patch”
（上記テーマの国際共同研究メタアナリシスへの参画）

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背景： 各種のガイドラインが循環器疾患（CVD）予測のための慢性腎臓病（CKD）、推定糸球体濾過率（eGFR）、尿アルブミン/クレアチニン比（ACR）の重要性を指摘している。しかし、これらを測定したコホートデータを用いた CVD 予測式作成が行われて以内ので、予測式に組み込まれていない。

仮説： 予測式である the AHA/ACC Pooled Cohort Equation (PCE) for atherosclerotic CVD (ASCVD)に CKD の指標を組み入れた CKD patch（Circulation 2017）の有用性を検証する。

方法： CKD patch は 2 つの要素を用いて外部データセットから較正を行った。すなわち、CKD 指標の予測値と実測値、および、CKD のハザード比である。CKD-PC の 13 コホートを用い、1 つのコホートで妥当性検討し、その後全 13 コホートを用いて最終の CKD patch を作成した。アウトカムは ASCVD（心筋梗塞と脳卒中）である。

結果： PCE に比べ、CKD patch は判別能と再分類能が向上した。最初に予測された ASCVD リスクに対する新たに較正された比の中央値は、CKD のとても高い、高い、適度のリスクでそれぞれ、1.57、1.29、1.13 であった。

結論： CKD patch は、CKD 指標を用いて、初めて ASCVD リスクを客観的に較正できることを示した。CKD の重症度に応じて、CKD 患者の 5-25%が高リスクに再分類された。

“CKD patch” to incorporate kidney disease measures into the AHA/ACC Pooled Cohort Equation: an international individual-level data study from the CKD Prognosis Consortium (CKD-PC)

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Background: Major guidelines emphasize measures of chronic kidney disease (CKD), estimated glomerular filtration rate (eGFR) and urine albumin-to-creatinine ratio (ACR), as cardiovascular disease (CVD) risk enhancers but often fail to specify how to incorporate them, partly because of missing CKD data in datasets from which prediction models are derived for these guidelines.
Hypothesis: Our new approach, “CKD patch” (Circulation 2017;136:A16426), will usefully incorporate CKD measures into the AHA/ACC Pooled Cohort Equation (PCE) for atherosclerotic CVD (ASCVD) risk prediction without refitting traditional predictors and CKD measures in PCE-deriving datasets.
Methods: “CKD patch” calibrates predicted risk from a base model using two elements from external datasets: 1) the difference in observed vs. expected values of CKD measures; and 2) hazard ratios for CKD. In 13 cohorts in CKD-PC (n=101,145 without prevalent CVD), we cross-validated the development of “CKD patch” by selecting one cohort at a time as a validation dataset and then developed the final “CKD patch” using all 13 cohorts. The outcome was incident ASCVD (myocardial infarction and stroke).
Results: Compared to the recalibrated PCE, “CKD patch” improved discrimination (cross-validated Δc-statistic 0.006 [95%CI 0.003-0.010]) and reclassification (net reclassification index 0.034 [0.024-0.044]). Median (interquartile range) ratio of newly calibrated to originally predicted ASCVD risk with the final “CKD patch” was 1.57 (1.52-1.63), 1.29 (1.27-1.31), and 1.13 (1.11-1.16) for CKD at very high, high, and moderate risk, respectively (Figure). In each CKD category, 24%, 12%, and 4.6% were reclassified from intermediate to high ASCVD risk.
Conclusions: “CKD patch” provides for the first time an option to objectively calibrate ASCVD risk using CKD measures without refitting in underlying datasets. Depending on CKD severity, 5-25% of persons with CKD are reclassified as high risk using CKD data.

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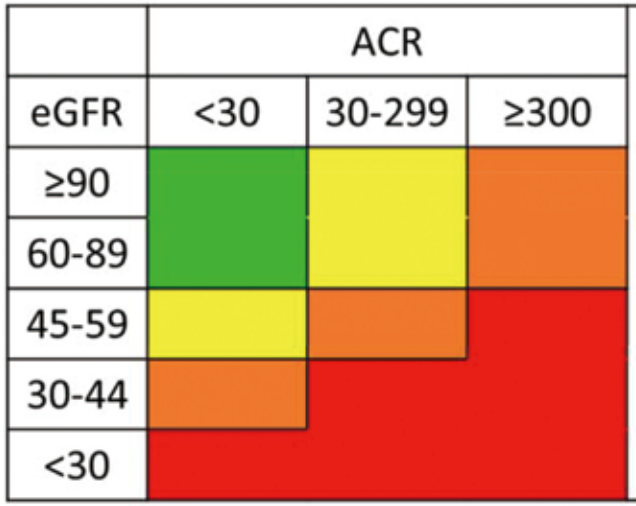
Figure. CKD stages and median (interquartile interval) ratio of newly calibrated predicted risk with "CKD patch" to originally predicted risk with AHA/ACC PCE as well as proportion of individuals reclassified to high 10-y ASCVD risk with "CKD patch"



CKD stages	"patch" to original ratio	Reclassification to high risk
No CKD	0.99 (0.97, 1.00)	0.7%
CKD at moderate risk	1.13 (1.11, 1.16)	4.6%
CKD at high risk	1.29 (1.27, 1.31)	11.6%
CKD at very high risk	1.57 (1.52, 1.63)	24.2%