4. **Pulse Oximetry screening for congenital heart defects in newborn infants (PulseOx): a test accuracy study.** Ewer AK, Middletonn LJ, Furmston AT, et al, on behalf of the PulseOx Study Group. Lancet 2011;378:785–94.
doi: 10.1016/S0019-4832(12)60028-5

Antenatal ultrasonography and postnatal clinical examination are the current standard methods of screening for congenital heart disease (CHD); however, life-threatening defects often are not detected. This large multicentric prospective study from UK assesses the accuracy of pulse oximetry as a screening test for congenital heart defects.

In six maternity units in the UK, 20,055 asymptomatic newborn babies (gestation >34 weeks) were screened with pulse oximetry before discharge. Infants who did not achieve predetermined oxygen saturation thresholds underwent echocardiography while all others were followed up to 12 months of age. The main outcome was the sensitivity and specificity of pulse oximetry for detection of critical congenital heart defects (causing death or requiring invasive intervention before 28 days of life) or major CHD (causing death or requiring invasive intervention within 12 months of age). Fifty-three babies had major CHD (24 critical), a prevalence of 2.6 per 1000 live births. Analyses were done on all babies for whom a pulse oximetry reading was obtained. Sensitivity of pulse oximetry was 75% (95% CI 53.29–90.23) for critical cases and 49.06% (35.06–63.16) for all major congenital heart defects. Congenital heart defects were already suspected after antenatal ultrasonography in 35 cases and if these cases are excluded the sensitivity of pulse oximetry further reduced to 58.33% (27.67–84.83) for critical cases and 28.57% (14.64–46.30) for major defects. There were 169 (0.8%) false positive results (specificity 99.16%, 99.02–99.28) of which 6 cases were significant, but not major congenital heart defects, and 40 were other illnesses that required urgent medical intervention.

Pulse oximetry is a safe and feasible test that adds value to existing screening. It identifies cases of critical congenital heart defects that go undetected with antenatal ultrasonography with an additional advantage of early detection of other diseases.

Perspective

It is important to detect major life-threatening congenital heart defects in time as sudden deterioration may occur in newborn babies with critical or major congenital heart defects. This is the largest study of its kind, by the National Institute of Health Research, United Kingdom and aims at assessing efficacy of pulse oximetry as a screening tool for congenital heart defects. In accordance with other recent studies, the results support the routine practice of pulse oximetry in neonates. The sensitivity of pulse oximetry is consistently proven to be from 50% to 80% which may not be acceptable for screening of potentially fatal major congenital heart defects. Furthermore, additional cost might explain current hesitation for widespread use of pulse oximetry of all newborns. In developing countries like India, where substantial numbers of deliveries are not supervised and occur outside the hospital the implementation remains an important issue. Furthermore, accuracy would be different in neonatal population where respiratory causes of desaturation are not uncommon. For pulse oximetry to be of utility, it is imperative to perform this test properly, preferably by using a plethysmograph which displays arterial waveform, lest errors of measurement may occur.

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1. **Rivaroxaban versus warfarin in nonvalvular atrial fibrillation**. Manesh R, Patel MD, Kenneth W, et al and the ROCKET AF Steering Committee for the ROCKET AF Investigators. N Engl J Med 2011;365:883–91. doi: 10.1016/S0019-4832(12)60029-7

Background: The use of warfarin reduces the rate of ischaemic stroke in patients with atrial fibrillation (AF) but requires frequent monitoring and dose adjustment. Rivaroxaban, an oral factor Xa inhibitor, may provide more consistent and predictable anti-coagulation than warfarin.
Methods: In a double-blind trial, the authors randomly assigned 14,264 patients with non-valvular AF who were at increased risk for stroke to receive either rivaroxaban (at a daily dose of 20 mg) or dose-adjusted warfarin. The per-protocol, as-treated primary analysis was designed to determine whether rivaroxaban was non-inferior to warfarin for the primary end point of stroke or systemic embolism.
Results: In the primary analysis, the primary end point occurred in 188 patients in the rivaroxaban group (1.7% per year) and in 241 in the warfarin group (2.2% per year) (hazard ratio in the rivaroxaban group, 0.79; 95% confidence interval [CI], 0.66–0.96; $P<0.001$ for non-inferiority). In the intention-to-treat analysis, the primary end point occurred in 269 patients in the rivaroxaban group (2.1% per year) and in 306 patients in the warfarin group (2.4% per year) (hazard ratio, 0.88; 95% CI, 0.74–1.03; $P<0.001$ for non-inferiority; $P=0.12$ for superiority). Major and non-major clinically relevant bleeding occurred in 1475 patients in the rivaroxaban group (14.9% per year) and in 1449 in the warfarin group (14.5% per year) (hazard ratio, 1.03; 95% CI, 0.96–1.11;

$P=0.44$), with significant reductions in intracranial haemorrhage (0.5% vs 0.7%, $P=0.02$) and fatal bleeding (0.2% vs 0.5%, $P=0.003$) in the rivaroxaban group.
Conclusion: In patients with AF, rivaroxaban was non-inferior to warfarin for the prevention of stroke or systemic embolism. There was no significant between-group difference in the risk of major bleeding, although intracranial and fatal bleeding occurred less frequently in the rivaroxaban group.

2. **Apixaban versus warfarin in patients with atrial fibrillation.** Granger CB, Alexander JH, McMurray JJ, ARISTOTLE Committees and Investigators. N Engl J Med 2011;365:981–92. doi: 10.1016/S0019-4832(12)60030-3

Background: Vitamin K antagonists are highly effective in preventing stroke in patients with atrial fibrillation (AF), but have several limitations. Apixaban is a novel oral direct factor Xa inhibitor that has been shown to reduce the risk of stroke in a similar population in comparison with aspirin.
Methods: In this randomised, double-blind trial, we compared apixaban (at a dose of 5 mg twice-daily) with warfarin (target international normalised ratio [INR], 2.0–3.0) in 18,201 patients with AF and at least one additional risk factor for stroke. The primary outcome was ischaemic or haemorrhagic stroke or systemic embolism. The trial was designed to test for non-inferiority, with key secondary objectives of testing for superiority with respect to the primary outcome and to the rates of major bleeding and death from any cause.
Results: The median duration of follow-up was 1.8 years. The rate of the primary outcome was 1.27% per year in the apixaban group, as compared with 1.6% per year in the warfarin group (hazard ratio with apixaban, 0.79; 95% confidence interval [CI], 0.66–0.95; $P<0.001$ for non-inferiority; $P=0.01$ for superiority). The rate of major bleeding was 2.13% per year in the apixaban group, as compared with 3.09% per year in the warfarin group (hazard ratio, 0.69; 95% CI, 0.60–0.80; $P<0.001$), and the rates of death from any cause were 3.52% and 3.94%, respectively (hazard ratio, 0.89; 95% CI, 0.80–0.99; $P=0.047$). The rate of haemorrhagic stroke was 0.24% per year in the apixaban group, as compared with 0.47% per year in the warfarin group (hazard ratio, 0.51; 95% CI, 0.35–0.75; $P<0.001$), and the rate of ischaemic or uncertain type of stroke was 0.97% per year in the apixaban group and 1.05% per year in the warfarin group (hazard ratio, 0.92; 95% CI, 0.74–1.13; $P=0.42$).
Conclusion: In patients with AF, apixaban was superior to warfarin in preventing stroke or systemic embolism, caused less bleeding, and resulted in lower mortality.

Perspective

Atrial fibrillation is the most prevalent sustained arrhythmia affecting aging population. One of the most important aims of managing AF is to prevent embolic stroke. Oral anti-coagulation with vitamin K antagonist has been shown to be very effective in achieving this goal and has been used for long time now. Although very effective, this needs frequent monitoring and dose adjustment. Besides the drug and food interactions are very common, making the dose adjustments very important. Bleeding complications related to oral anti-coagulation in addition to the above mentioned difficulties make physicians extremely cautious while prescribing these very important drugs especially elderly in India. With limited high quality pathology laboratory set up in the semi-urban and rural India physicians many a time refrain from prescribing oral anti-coagulants for AF. Advent of oral Xa inhibitors mark a new era in management of patients requiring oral anti-coagulation. These drugs are given in fixed dose, have shorter half-lives and have limited interactions with other drugs and food. The two recent studies ROCKET AF and ARISTOTLE done with rivaroxaban and apixaban indicate the potential of these drugs. Both studies included large number of patients treated with either of the drug and followed up for approximately 2 years. Most importantly, both these studies used the established therapy, i.e. warfarin as the comparator drug. This puts both the studies on a very high pedestal. ROCKET AF study showed non-inferiority of rivaroxaban to warfarin in preventing stokes and systemic embolism. Incidence of bleeding was same although intracranial bleeding and fatal bleeding was less with rivaroxaban. In ARISTOTLE, apixaban reduced strokes and bleeding compared to warfarin when tested in >18,000 patients for mean 1.8 years. Both these studies usher in a new era of drugs for stoke prevention in AF. The beauty of these drugs lies in fixed drug dose requiring no monitoring of the drug effect as against warfarin. Frequent international normalised ratio (INR) monitoring with dose adjustment has been the main hurdle in using warfarin especially in countries like ours. The only question for us would be the cost of the new drugs as the therapy is long-term. If the industry can offer factor Xa inhibitors at a cost which is feasible for long-term use in most of the patients; stoke prevention in AF can change from dream to reality. However, a word of caution is that these drugs are predominantly excreted through kidneys and therefore one has to be careful while prescribing to patients with chronic kidney disease (CKD).

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