Does a prolonged QT peak identify left ventricular hypertrophy in hypertension
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Record Status
This is a critical abstract of an economic evaluation that meets the criteria for inclusion on NHS EED. Each abstract contains a brief summary of the methods, the results and conclusions followed by a detailed critical assessment on the reliability of the study and the conclusions drawn.

Health technology
The comparison of different electrocardiography criteria for risk-stratifying hypertensive patients with left ventricular hypertrophy (LVH), in order to perform an echocardiogram. The criteria compared were QT peak of lead I, the usual Sokolow-Lyon "voltage criteria", the Cornell Voltage criterion and the Cornell Product criterion. QT peak was defined as the onset of QRS to the peak of the T wave. The usual Sokolow-Lyon voltage criteria were defined as S in V1 + R in V5 or V6 > 3.5 mV. The Cornell Voltage criterion was defined as R in aVL plus S in V3. It is positive for LVH if it is superior or equal to 2.8 mV in male patients and 2 mV in female patients. The Cornell Product is a product of the Gender Specific Cornell Voltage and the mean QRS duration. If the Cornell Product is superior or equal to 243.6 mV.ms, then it is positive for LVH.

Type of intervention
Screening and diagnosis.

Economic study type
Cost-effectiveness analysis.

Study population
The study population comprised hypertensive patients who were either treated or had been withdrawn from antihypertensive medication for at least 7 days. Patients with ischaemic and cerebrovascular diseases, or with previous accelerated hypertension where drug treatment could not be safely discontinued, were excluded. Also excluded were patients with evidence of myocardial ischaemia on exercise electrocardiogram (ECG) and patients with echocardiographic evidence of valvular heart disease. Patients who had atrial fibrillation or flutter, bigeminy, paced rhythm, or bundle branch block on their ECG were also excluded, as these ECG changes tend to make the QT interval difficult to measure reliably.

Setting
The setting was primary and secondary care. The economic study was carried out in Ninewells Hospital, Dundee, UK.

Dates to which data relate
The dates to which the effectiveness evidence and resource use data related were not reported. The price year was not reported.

Source of effectiveness data
The effectiveness data were derived from a retrospective single study.

Link between effectiveness and cost data
The costing was performed on the same patient sample as that used in the effectiveness study.
Study sample
Forty-seven hypertensive patients referred to a hospital-based hypertension unit were selected. The mean age was 46 years (range: 20 - 67) and 31 patients were male (66%). The patients had a mean blood pressure of 161.7/99.3 mmHg, and all had normal LV systolic function as indexed by fractional shortening (mean FS=38, range: 26 - 51). No power calculations were reported.

Study design
This was a retrospective, cross-sectional observational study that was conducted in a single centre. All the patients had both an ECG and an echocardiogram to estimate their left ventricular mass index (LVMI). A single operator conducted the echocardiographic examinations. The ECGs were analysed by a different single observer who was blind to the outcome of the echocardiogram and clinical findings. LVH was defined as an LVMI greater than or equal to 134 g/m2 in men and 110 g/m2 in women. The heart-rate corrected QT peak of all the leads which could be digitised were calculated using Bazett's formula. Of the 47 patients, 24 had LVH diagnosed by echocardiography.

Analysis of effectiveness
The main effectiveness outcomes assessed were the sensitivity and specificity of the tests for different cut-off values of QT peak to predict LVH, using a receiver operating characteristic curve. Statistical tests were performed to analyse correlations and statistical significance for LVH and LVMI and the various QT indices and ECG criteria. The Mantel-Haenszel common odds ratio was also computed with 95% confidence intervals. Inter-observer reproducibility was estimated in 15% of the ECGs.

Effectiveness results
The heart-rate corrected QT peak of lead I was significantly correlated with LVMI (Spearman correlation coefficient 0.45, two-tailed p=0.002; n=44). This correlation was also significant in lead aVR (Spearman correlation coefficient 0.43, two-tailed p=0.004).

The cut-off value of 314 ms yielded a sensitivity of 71% and a specificity of 70% at diagnosing LVH. LVH was likely to be present if QT pc in lead I was superior or equal to 320 ms (odds ratio 5, 95% confidence interval: 1.4 - 18). This corresponded to a sensitivity of 63% and a specificity of 80%.

If all patients with heart-rate corrected QT peak superior or equal to 300 ms were given an echocardiogram, then no cases of LVH would be missed (100% sensitive, 50% specific).

The positive and negative predictive values of heart rate corrected QT peak in lead I were superior to the classic voltage criteria (Sokolow-Lyon criteria) at diagnosing LVH.

The Cornell Voltage and Cornell Product criteria had excellent positive predictive values (100%). However, it could be argued that their sensitivities were rather low, with a negative predictive value of 51% only, leading to 92% of LVH cases being missed.

Clinical conclusions
The main finding of this study was that the heart-rate corrected QT peak in lead I not only correlated with the LVMI, but also appeared to correlate more strongly with LVMI than the classic QT end dispersion. Also, that the usual "voltage criteria" (S in V1 + R in V5 or V6 >3.5 mV) performed less well in terms of both positive and negative predictive values in the diagnosis or exclusion of LVH than the proposed ECG criterion heart-rate corrected QT peak of lead I >/= 300 ms.

Measure of benefits used in the economic analysis
The number of LVH cases detected was used as the benefit measure. This measure was derived from the effectiveness
Direct costs
The direct cost included was the hospital's average cost of performing an echocardiogram. This was based on personal communications. The ECG cost was not included, as it was considered that all hypertensive patients should have an ECG at some point. Discounting was not carried out, which was appropriate because of the short-term horizon of the study. Since the only cost was that of echocardiograms (one per patient), the authors did not report any other quantities or costs. The quantities and the costs were estimated from actual data, although the authors stated that the costs of diagnostic tests varied between laboratories because of the methods used to account for fixed costs of tests. The dates relating to the quantity of resources measured and price year were not reported.

Statistical analysis of costs
No statistical analysis of the costs was reported.

Indirect Costs
No indirect costs were reported.

Currency
UK pounds sterling (GBP).

Sensitivity analysis
No sensitivity analysis was reported.

Estimated benefits used in the economic analysis
Twenty-four patients had LVH.

The usual voltage criteria resulted in 4% of cases being detected with LVH;
the Cornell Voltage and Cornell Product criteria resulted in 8% of cases being detected with LVH;
the QT end dispersion ≥ 50 ms criterion resulted in 66% of cases being detected with LVH;
the heart-rate corrected QT peak in lead I ≥ 320 ms criterion resulted in 62% of cases being detected with LVH;
the heart-rate corrected QT peak in lead I ≥ 300 ms criterion resulted in 100% of cases being detected with LVH; and
performing echocardiography in all hypertensive patients resulted in 100% of cases being detected.

Cost results
The total costs were:
11,750 for performing echocardiography in all hypertensive patients;
1,750 for the usual voltage criteria;
500 for Cornell Voltage;
500 for Cornell Product;
5,750 for QT end dispersion $\geq$ 50 ms; 
5,000 for heart-rate corrected QT peak in lead I $\geq$ 320 ms; and 
8,750 for heart-rate corrected QT peak in lead I $\geq$ 300 ms (n=47; 24 cases with LVH).

**Synthesis of costs and benefits**
Only the average costs per case detected were calculated. The cost per LVH case detected using different criteria for echocardiography was:

- 490 for performing echocardiography in all hypertensive patients;
- 1,750 for the usual voltage criteria;
- 250 for Cornell Voltage and for Cornell Product;
- 360 for QT end dispersion;
- 333 for heart-rate corrected QT peak in lead I $\geq$ 320 ms; and
- 364 for heart-rate corrected QT peak in lead I $\geq$ 300 ms.

**Authors’ conclusions**
Measuring the heart-rate corrected QT peak in lead I had higher predictive values than the usual voltage criteria, and was a cost-effective way of identifying hypertensive patients who were likely to have echocardiographic left ventricular hypertrophy (LVH).

**CRD COMMENTARY - Selection of comparators**
The choice of the different ECG criteria and the echocardiographic screening for LVH was justified because they are widely available and reflect standard practices in the authors’ setting. You should judge whether these screening methods are relevant in your setting, or whether other comparators could also have been relevant, including those chosen for the study.

**Validity of estimate of measure of effectiveness**
The study was based on a retrospective cohort design. This was appropriate for the study question since it would allow the identification of a very large number of patients, making the results of the study more generalisable. However, the study included only 47 patients and no power calculations were reported. Thus, the sample size might have been too small to address appropriately the sensitivity and specificity of each screening strategy. In addition, the exclusion criteria were numerous. Therefore, the small sample might not have been representative of the study population. Although the authors reported that statistical analyses were undertaken to account for potential biases and confounding factors, such analyses were not reported.

**Validity of estimate of measure of benefit**
The estimation of benefits was obtained directly from the effectiveness analysis. The health benefit measure used (the number of cases detected) limits the comparability to other economic valuations in other health fields.

**Validity of estimate of costs**
Although the authors reported that the perspective of primary care was used in the economic analysis, as the analysis included the cost of echocardiography based on a hospital average cost, the actual perspective adopted appears to have been that of the health care system. Therefore, some relevant costs could have been omitted from the analysis (e.g.
physician fees, costs of missed cases of LVH). The costs and the quantities were not reported separately, which would not allow the analysis to be easily extrapolated to other settings. Statistical and sensitivity analyses of the costs were not reported. The price year was not reported, which will make any future reflation exercises difficult. These factors affect the robustness of the costs results. Discounting was not necessary since all the costs were incurred during a two-year period.

Other issues
The authors compared some of their findings with those from other studies. They did not directly address the issue of the generalisability of the results to other settings, but they did acknowledge some limitations of their study. For example, the small sample size, and the perspective and costs used. The authors also acknowledged that it would be useful to consider different patient groups, such as hypertensive patients with ischaemic heart disease, cerebrovascular disease, asymptomatic hyperthyroidism, chronic renal failure and others.

Implications of the study
The authors reported that, if the results of this pilot study are confirmed in a larger study, then QT peak measurements could become an inexpensive screening test for LVH in hypertension.

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