hypothesis. Moreover, sympathetic overactivity is a key component of the signaling pathways altered in hypertension-related cardiac remodeling. However, in the LIFE study and other related meta-analysis, antihypertensive treatment with beta blocker-based therapy resulted in less LVH regression than an ACEI or ARB-based strategy. The diminished efficacy of beta-blockers on LVH reduction might reside in their inability to decrease myocardial fibrosis. In contrast, RD strategy has shown significant LVH regression and improvement of diastolic function. It has also been noted that RD-induced LVH regression was not exclusively associated with BP reduction.

However, the number of patients involved in this trial was small and the follow up duration was only 6 months. Furthermore, no comparator therapy was available for this group of resistant hypertension patients. A role for the sympathetic nervous system in long-term control of body fluid volumes and arterial pressure is controversial for several reasons, including the difficulty in assessing the functional effects of the renal nerves under chronic conditions. A key issue with this RF energy denervation approach is whether anatomical and/or functional re-growth of renal sympathetic nerves occur, abrogating the long term BP-lowering benefits. Such re-growth has been observed in other conditions where sympathetic nerves have been disrupted, such as in organ transplantation. A large randomized controlled trial with long-term follow up is required.

**ALTITUDE halted: Adverse events when aliskiren added to ACEI, ARB therapy.**

**ALTITUDE study**

**Background:** Patients with type 2 diabetes are at increased risk of macro- and microvascular disease, and the presence of albuminuria and/or reduced kidney function further enhances macrovascular risk. ACEI reduce both macro- and microvascular events, yet the residual renal and cardiovascular risk still remains high. Aliskiren a novel oral direct renin inhibitor that unlike ACEI and ARBs, lowers plasma renin activity, angiotensin I and angiotensin II levels, may thereby provide greater benefit compared to ACEI or ARB alone.

**Methods:** The primary objective of the ALTITUDE trial was to determine whether aliskiren 300 mg once daily, reduces cardiovascular and renal morbidity and mortality compared with placebo when added to conventional treatment (including ACEI or ARB). ALTITUDE was an international, randomized, double-blind, placebo-controlled, parallel-group study, which included three categories of high-risk patients with type 2 diabetes (aged ≥ 35 years): those with either urinary albumin/creatinine ratio (UACR) ≥ 200 mg/g; microalbuminuria (UACR) ≥ 20–<200 mg/g and eGFR ≥ 30–<60 mL/min/1.73 m²; and thirdly, those with a history of cardiovascular disease and eGFR ≥ 30–<60 mL/min/1.73 m² with or without microalbuminuria. ALTITUDE was an event driven trial that aimed to randomize 8600 patients with a planned follow-up time of 48 months. The primary outcome measure was time to first event for the composite endpoint of cardiovascular death, resuscitated death, myocardial infarction, stroke, unplanned hospitalization for heart failure, onset of end-stage renal disease or doubling of baseline serum creatinine concentration. Secondary endpoints included a composite CV endpoint and a composite renal endpoint.

**Perspective**

The trial was prematurely halted by data safety and monitoring board (DSMB) as there was an increase in adverse events and no apparent benefits among patients randomized to aliskiren.

In making its recommendation, the DSMB noted that the active-treatment group experienced an increased incidence of nonfatal stroke, renal complications, hyperkalemia, and hypotension over 18–24 months of follow-up. The committee concluded that patients were unlikely to benefit from aliskiren on top of standard antihypertensive therapy.

Though earlier this year, ACCELERATE trial looking at aliskiren in combination with a calcium-channel blocker showed positive results and the FDA had approved both a dual- and triple-combination drug including aliskiren, but the recommended combination did not include an ACEI or ARB.

**ALTITUDE study** tried to evaluate the effect of direct renin inhibition in diabetic patients who are likely to experience the compensatory rise in plasma renin and other downstream RAAS components, including aldosterone, induced by ACEI or ARBs. The damaging impact of aldosterone escape is well established in CVD and renal disease during ACEI or ARB treatment. Aliskiren was expected to block the compensatory rise in RAAS activity, and offer a novel approach to dual blockade of the RAAS. Although recent results of both VALIANT and ONTARGET showed no clinical benefits of the combination of effective doses of an ACEI and ARB, it was presumed combining either of them with aliskiren would offset potential deleterious effects of compensating rennin activation. However, the results of ALTITUDE study showed the combination to be detrimental.

Contributed by  
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Editor's perspective

This large multinational study shows that performing a calcium scoring in a patient undergoing a CTA does not provide additional information in terms of risk assessment. Even a calcium score of 0 can have a significant event rate if there is a noncalcified plaque of more than 50%. Hence a contrast CTA is important to clearly delineate the presence or absence of CAD.


Objectives: Does a coronary CTA strategy in patients presenting with chest pain in the ER lead to a safe early discharge strategy with a low cardiac event rate on follow up?

Editor's perspective

This large multicentre nonindustry sponsored trial was conducted at five centres in the US with a prime objective of demonstrating the accuracy and safety of using a CTA based strategy in patients with intermediate probability of chest pain.

The rationale to conduct the study was the high rate of noncardiac causes found among patients with possible acute coronary syndromes.

Two groups were randomly assigned patients one to a CTA strategy and the other to a traditional strategy. The primary outcome was the absence of MI and cardiac death in the first 30 days after presentation.

1370 subjects were enrolled. Of the 640 patients with a negative CTA exam none had a primary outcome. The patients in the CTA group had a higher rate of discharge (49.6% vs 22.7%), a shorter length of stay (18 h vs 24.8 h) and a higher rate of CAD detection (9% vs 3.5%) with an adverse event in both groups.

In a real world setting the CTA based strategy for low to intermediate risk patients with possible acute coronary syndrome appears to allow the safe discharge of patients from the ER. This strategy can be replicated in our country as the number of coronary enabled scanners are increasing and so is the number of physicians who are able to assess coronary stenoses on CTA.

Contributed by
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Introduction: Epidemiology of sudden cardiac death (SCD) in India is understudied.

Methods: We assessed proportion of SCD among total mortality in a population in Southern India using a staged, questionnaire-based kindred-wide approach. Detailed questionnaires (DQs) were completed by medical trainees from 8 medical colleges. Preliminary questionnaires evaluated total deaths in the kindred of a respondent. Deaths due to obvious non-cardiac causes were excluded. DQs were completed for the remaining deaths and categorized using a three-member adjudication system.

Results: A total population of 22,724 was evaluated by 478 respondents (278 M and 200 F). Out of a total of 2185 deaths, 1691 (77.4%) were recallable. A total of 173 (10.3%; 128 M and 45 F; mean age – 60.8 ± 14 years) deaths were adjudicated as SCD. Of these, 82 (47.3%) were ≤60 years of age. Prior MI, LV dysfunction and prior aborted SCD were found in 33.5%, 22.5% and 5.7% respectively. Coronary artery disease (CAD) was observed in 66 (38%) and acute myocardial infarction documented in 30 (17%). At least 1 of 3 CAD risk factors – hypertension, diabetes, or smoking was observed in 80.6%.

Proportion of subjects with at least one risk factor for CAD were similar in the age groups above and below 50 years (67.6% vs. 81.7%, p = 0.065).

Conclusions: SCD contributed to 10.3% of overall mortality in this population from Southern India. On an average, SCD cases were 5–8 years younger compared to populations reported in the western hemisphere, with a high prevalence of major risk factors for CAD.

Perspective

The epidemiology of sudden cardiac death (SCD) is imprecise even in developed countries with electronic records and national indexing of deaths. Given the lack of medical records, innovative methods have been used to classify the cause of death like a ‘verbal autopsy’, i.e ‘a systematic retrospective inquiry of family members about the symptoms and signs of illness prior to death’. In this article, Rao et al. reported a large population-based study which surveyed the incidence of SCD through the novel use of staged detailed questionnaires in Southern India. Through these questionnaires administered to family members of medical students, a population of 22,724 was surveyed and a sample of 2185 deaths was obtained. Deaths were categorized by a 3-member adjudication system. They found that SCD contributed to 10.3% of total mortality. The mean age of the SCD population was 60.8 ± 14 years (35–85 years) and 55.5% of them were in the age group 50–70 years. Coronary artery disease (CAD) was found in 38% and 17% had documented acute myocardial infarction but only about 10% of them underwent revascularization. In the SCD cohort, 80.6% had at least one of the risk factors – diabetes, hypertension or smoking and this proportion was similar in subjects aged above and below 50 years. Amongst the SCD