Advocating the Need for a CT Coronary Angiography Screening Program for Prevention of Coronary Artery Disease in High – Risk Population & guiding future pharmaceutical research

Abhinav Aggarwal*
Department of Radiology, Mata Chanan Devi Hospital, India

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*Corresponding author: Abhinav Aggarwal, Junior Consultant Radiologist, Department of Radiology, Mata Chanan Devi Hospital, Block C, Janak Puri, New Delhi, India

Abstract

Cardio-vascular disease (CVD) is one of the major causes of morbidity and mortality in Europe and world. It accounts for majority of spend on healthcare in European Union countries and is the second on the list. Non-calcific plaques form the majority of plaques and non-calcific & mixed plaques are responsible for majority cases of severe stenosis. Since non-calcific and mixed plaques are resolvable by intensive statin therapy and are responsible for majority of severe acute coronary related events (vulnerable plaques), coronary artery disease is preventable if proper screening is done which should lead to significant decrease in economic burden of cardio-vascular & cerebro-vascular diseases. These findings warrant a discussion on systemic screening program for the same through CT coronary angiography.

Abbreviations: CVD: Cardio-vascular disease; EU: European Union; EHN: European Heart Network; A&E: accident & emergency; GPs: General practitioners; CTCA: Computed Tomography Coronary Angiography screening

Introduction

Cardio-vascular disease (CVD) is one of the major causes of morbidity and mortality in Europe and world [1]. Spectrum of cardio-vascular disease includes coronary artery disease, high blood pressure, angina, heart attack, congenital heart disease and stroke along with heart valve disease and cardiomyopathy [2]. The latest figures for 2017 issued by European Society of Cardiology show that every year 6 million new cases of CVD are introduced in European Union (EU) alone with a total of 11 million cases in whole of Europe. The figures for these have been increasing every year despite the introduction of lifestyle modifications including better diets and increasing exercise in daily routines. All these diseases lead to impairment of a large amount of man-force leading to high cost of the EU economy [3].

Etiology/Disease Burden Of CVD

Traditionally various lifestyle components like smoking, alcohol consumption and blood levels of cholesterol have been the main factors related to increased incidence of CVD [3,4]. In recent decades effect of genetic factors like overweight/obesity and diabetes have increased and is expected to increase further in coming decades [3,5]. As per the European Heart Network (EHN) statistics of 2015, incidence of diabetes has increased by 50% in last ten years. Despite successful implementation of various lifestyle changes like higher consumption of vegetables & fruits, decrease in smoking and increase in physical activity there has been an increase in incidence of CVD. This is because incidence of obesity has increased along with increased genetic predisposition to diabetes [5]. Even though mortality due to CVD is falling in Europe, it is second only to cancer in terms of morbidity and mortality worldwide. CVD is responsible for 45% all deaths in the Europe and is the main cause of death in men in all but 12 countries of Europe and in women in all but two countries in Europe. 3.9 million People die because of CVD in Europe and 1.8 million in EU [3]. This means that the number of deaths every year is almost one-fourth of new diagnosed cases
every year. The increased incidence of CVs has also led to a higher
diseased generation.

Pathogenesis Of CVD

The primary causative factor in the disease process of coronary
artery disease is atherosclerosis. Atheromas are formed in wall of
arteries due to gradual deposit of fatty material. These cause luminal
narrowing of arteries leading to decreased supply of oxygen-rich
blood to the heart [4]. Plaques can be classified into – fatty, calcific and
mixed. These are not an outcome of ageing phenomenon and in fact
the most common coronary plaque i.e. coronary calcium, has been
classified by AHA as type Vb atherosclerosis [6-8]. Several studies have
emphasized on the significance of coronary calcium in relation
to future coronary artery disease/CVD. Coronary calcium has shown
to be a better predictor of future CVD than the electrocardiogram,
echocardiography, stress echocardiography etc. Calcium score is
also independent of dyslipidemia in prognostication of CVD [9-
15]. The ability of vulnerable plaques to cause severe heart attack
leading to increased morbidity and mortality in recent decades has
been well documented [16]. Vulnerable plaques are lipid rich, show
positive remodeling, have spotty calcification and show napkin
ring sign on CTA. Traditionally Framingham risk score has been
used for prediction of CVD in various populations. It is the largely
a function of age & sex and is outdated in the presence of present
knowledge of CVD. Broadly speaking Framingham risk score says
that treat all men aged 60 years and don’t treat any women till
they are 60 years [17]. This leads to considerable overlap between
patients at risk and not at risk of CVD events.

Cost of CVD

CVD has been attributed to be the largest cause of mortality and
morbidity and premature death along with reduced quality of life
for the citizens of EU by the Council of Ministers of the European
Union [18]. Coronary artery disease and cerebrovascular disease
account for majority of CVD related deaths [19]. CVD is estimated
to cost EU economy approximately 210 billion euros a year. This
includes 111 billion euros (around 53%) in health care costs, 54
billion euros (approx. 26%) due to productivity losses and 45
billion euros (approx. 21%) due to informal care of the people
with CVD [3]. The healthcare expenditure includes: primary care,
accident & emergency (A&E) care, hospital patient care, outpatient
care and medications. Primary care includes CVD related visits to
general practitioners (GPs), together with GPs visits to patients
homes and where available visits to or by primary care nurse.
Specialist consultations taking place in out-patient wards, clinics or
patient’s homes were included in hospital outpatient care. Whereas
hospital inpatient care was calculated according to the number of
days in hospital including both case admissions and rehabilitation
sessions. Various trivial expenses like patient travel costs, out of
pocket expenses (eg. Child care, home aids and over the counter
medication) were clubbed under non-heath service costs [20].
Similarly cost of CVD in USA & Canada is estimated to be approx.
296 billion euros & 21.2 billion dollars respectively [21,22]. The
population of EU is 510.1 million [23], which make the cost of CVD
as more than 411.6 euros per person per year. On per capita basis
this is even more than cost of cancer to the EU and Europe as a
whole [24].

Taking Inspiration From Other Successfully Implemented
Screening Programs

One of the most successfully implemented healthcare-
screening programs in the world has been the various Breast
Cancer Screening program. Various studies conducted in various
countries have highlighted the survival & quality of life benefits of
these programs [25-27]. These studies range from being published
in 1991 to 2016 show that a properly planned breast cancer-
screening program is beneficial for more than 25 years. One of the
primary reasons behind the successful implementation of these
programs has been careful selection of screening population along
with regular assessment of the program characteristics. These
programs have constantly evolved/ modified over time based on
the results of previous years. The screening population has been
changed multiple times in various countries to make the programs
more cost-effective as well as maintaining their healthcare benefit
[25-27]. One of recent study published the economic analysis of the
breast cancer-screening program. This study aimed at analyzing the
cost-utility analysis of breast cancer screening program over a 20-
year period considering its utility accounting for the breast cancer-
screening period between the ages of 50-70 years. Quality-adjusted
life year/s was calculated. The authors found that even in the worst-case
scenario the screening program proved to be beneficial [28].
Considering the increasing incidence of CVD inspiration should
be taken from successfully implemented breast cancer-screening
program to propose a similar computed tomography coronary
angiography screening (CTCA) program for high-risk population.

Role of Statins And Ideas For Further Pharmaceutical
Research

Recently the head of a prominent cardiac association aged 52
years suffered a heart attack and was diagnosed with a blocked
coronary artery [29]. He is likely to have followed the guidelines of
cardiac association but suffered a heart attack due to high genetic
predisposition. Studies have shown that fatty and/or mixed plaques
can be reduced upto 30% in size by use of high-dose statins [30,31].
Even a mild plaque has a 6 times higher mortality for patients with
triple vessel involvement [32-38]. This is where the role of a well-
planned screening program becomes imperative. The aim is to
identify asymptomatic individuals at risk. Asymptomatic high-risk
individuals who are detected with non-significant coronary plaques
can be treated using statins to decrease the plaque load.

Cost of Prospected Screening Program

A major factor involved in implementing any healthcare
screening is financial cost. With a population of 743.1 million in
Europe the cost of any screening program is expected to be high.
However if a screening program is exquisitely planned and properly
executed can lead to long-term decrease not only in mortality & mortality caused due to CVD but the financial cost of CVD also. It may be important to note here that even if the cost of implementing a screening program equals the reduction in cost of CVD, the addition of life years and quality of life will be worth the effort. The cost of running a CVD screening program including Cardiac CT study shall include – cost of equipment (optimum CT scanners), qualified radiologists, adequately trained technicians and other supporting staff. Considering the variables involved the easiest to implement is coronary calcium scoring of high-risk individuals. A satisfactory coronary calcium score can be done on a 16-slice CT scanner [39]. Many studies have shown the role of vulnerable fatty/mixed plaques in younger high-risk population. The CVD caused as a result of vulnerable plaque cause higher morbidity and mortality [40]. These plaques are not detected on CT coronary calcium study and require contrast-enhanced angiography study to optimum quantification. Therefore rather than CT calcium scoring a CTCA study would be more beneficial for this group of population.

The screening test needs to be – fast, reliable, accurate and non-invasive. It should rule out CAD, aid in diagnosis (extent & severity and anatomical & flow limiting), predict outcome, guide management and exclude non-cardiac causes of chest pain. One of the salient benefits of CTCA is its high negative predictive value. A person diagnosed with a normal CTCA study is practically not susceptible to a heart attack for next few years [41,42]. This can help to segregate the screening population further such that a person with a normal CTCA study can be excluded from another CTCA for a certain period to reduce the cost of screening program. CTCA can diagnose completely occluded ramus intermedius, which is missed on catheter angiography and is even better for chronic total occlusions because of better visualization of collaterals. CTCA can help in treatment management for intervention by telling calcification, lesion length, blunt stump, bending and kinking [43,44]. Various software’s are available which help reduce inter-observer variability in detection and quantification of vulnerable plaques [45-48]. CTCA can also provide information regarding myocardial ischemia and cardiomyopathies [49-52]. Studies have proved that only ischemia guided revascularization improves survival [53].

So if the level of risk as per CTCA is:

a) Very low – the patient just needs to be reassured,
b) Low – active prevention is required,
c) High – catheter angiography with possible stent placement is suggested,

Intermediate/non-assessable–stress/ischemia imaging should be carried out.

Traditional catheter angiography is not effective in using as screening tool. CTCA can now be effectively called as gate-keeper to catheter angiography laboratory. “Of all the forms of inequality, injustice in health is the most shocking and inhumane.” – Martin Luther King.

References

1. Non-calcific plaques form the majority of plaques and non-calcific & mixed.
3. European Society of Cardiology fact sheet.


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