Should All Patients Receive Statins to Reduce Cancer Risk After Heart Transplantation?

Noel W. Clarke, MBBS, ChM; Michael D. Brown, PhD

The predominant aim of statin therapy is the reduction of cholesterol to less harmful levels, but this may not be the means by which anticancer properties are effected. This notion is supported by the data from the study by Frolich et al,1 which show that the cancer-reducing effect was not related in any way to the absolute levels of serum cholesterol. This is not particularly surprising. As the authors emphasize, statins have pleiotropic anticancer effects, one of the most important being 3-hydroxy-3-methylglutaryl coenzyme A (HMG-CoA)–related inhibition of the Mevalonate pathway, a fundamentally important cancer pathway whose blockade results in disruption of neoplastic processes such as initiation of cancer growth2 and, in particular, the cellular migrational behavior which is responsible for cancer progression and metastasis.4 There is controversy among cancer experts as to whether the cholesterol-lowering effect is important, but in fact the critical inhibitory action on cholesterol metabolism may be within lipid rafts, cellular membrane microdomains which harbor many receptors for cellular signaling and where statins such as Simvastatin are known to reduce cholesterol levels and impair lipid raft function. Their action here is known to inhibit cancer-related cellular signaling.5

In light of the evidence presented, is there a case for widespread use of statins as a cancer preventive in this important area of transplantation? It is important to keep a balanced perspective, given that this is a relatively small, single-center series and to bear in mind that statins do have side effects. It is also important to recognize that not all statins are equal: Lipophilic statins, in contrast to hydrophilic ones, have been shown to have differential modes of action,4,6 and this affects their anticancer properties in testing in vitro.4 Given that there is a good evidence base for the noncancer benefits of these drugs in cardiac transplantation, it seems unlikely that a randomized trial testing the use of statins against no statins will be possible. Perhaps the way forward, therefore, will be to follow Bayesian approaches in this area, consolidating this and other datasets to facilitate larger-scale and more sophisticated analysis to address the proposition that statins (of whatever type) should be used universally in heart transplant patients. For the moment, however, it may be safer to adopt a verdict of unproven, while recognizing the fact that in this study, as in many others, the statistical arrows relating to statins and their anticancer effect are pointing in a similar direction.

Disclosures

None.

References


Key Words: Editorials | lipids | surgery | transplantation
Should All Patients Receive Statins to Reduce Cancer Risk After Heart Transplantation?
Noel W. Clarke and Michael D. Brown

_Circulation_. 2012;126:391; originally published online July 3, 2012;
doi: 10.1161/CIRCULATIONAHA.112.121343

_Circulation_ is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 2012 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the
World Wide Web at:
http://circ.ahajournals.org/content/126/4/391

Permissions: Requests for permissions to reproduce figures, tables, or portions of articles originally published in _Circulation_ can be obtained via RightsLink, a service of the Copyright Clearance Center, not the Editorial Office. Once the online version of the published article for which permission is being requested is located, click Request Permissions in the middle column of the Web page under Services. Further information about this process is available in the Permissions and Rights Question and Answer document.

Reprints: Information about reprints can be found online at:
http://www.lww.com/reprints

Subscriptions: Information about subscribing to _Circulation_ is online at:
http://circ.ahajournals.org//subscriptions/