

## カルベジロールは乳がん女性の心臓を保護する (Abstract 18-LB-17722-ACC)

化学療法による心障害に対するβ遮断薬の心保護に関する結果は様々である

Beta-blocker shows mixed results in protecting against chemotherapy-induced heart damage

新たに乳がんと診断され化学療法施行中に心毒性保護目的でβ遮断薬カルベジロールを投与された患者を6か月追跡した結果、心機能低下についてはプラセボ群と差がなかった。しかし、カルベジロールを内服した患者は血漿トロポニンI上昇を来す確率が有意に低かった(41.6% vs. 26%)と、American College of Cardiology's 67th Annual Scientific Session で発表され、同時に *Journal of the American College of Cardiology* オンライン版に掲載された。

### Full Text

After six months of follow up, women newly diagnosed with breast cancer who were given the beta blocker carvedilol to prevent heart issues while undergoing chemotherapy showed no difference in declines in heart function compared with those taking a placebo. Patients who took carvedilol, however, were significantly less likely to have an elevated plasma levels of troponin I, according to a study presented at the American College of Cardiology's 67th Annual Scientific Session and simultaneously published online in the *Journal of the American College of Cardiology*.

The study enrolled 200 patients diagnosed with breast cancer who had normal left ventricular ejection fraction and who, as part of their cancer treatment, were scheduled to receive anthracycline (ANT).

Patients were randomly assigned to receive either carvedilol (median daily dose of 18.4 mg/day) or placebo when starting ANT chemotherapy (240 mg/m<sup>2</sup>) until completing it. ANT is a type of chemotherapy that at certain cumulative doses has been shown to cause heart damage by weakening the heart muscles. Carvedilol works by slowing the heart rate, opening blood vessels and improving blood flow, which also lowers blood pressure.

"This is the largest randomized clinical trial of a beta blocker to prevent the toxic effects of contemporary doses of anthracycline [ANT] on the heart," said Mônica Samuel Avila, MD, assistant doctor in the Heart Failure and Heart Transplant Department in Heart Institute, Clinical Hospital of Medical School of São Paulo, and the study's lead author. "This is only short-term follow up, but we found that carvedilol seems to prevent myocardial injury, but it did not have an impact on left ventricular ejection fraction."

Avila also said the study findings further reinforce the need for cardiologists and oncologists to work together to define the best treatment strategies for individual cancer patients that minimize other negative effects, especially to the heart. Neither the patients nor those administering the treatment knew which patients received carvedilol versus the placebo.

Researchers assessed cardiotoxicity by measuring heart function with periodic echocardiograms and blood test to check for high-sensitivity troponin T, which is released into the bloodstream when injury to the heart occurs. These measures were tracked at baseline and after each cycle of ANT chemotherapy (three, six, nine and 12 weeks) and after the end of all chemotherapy (around 24 weeks). Patients in the carvedilol and placebo groups were an average of 51 and 53 years of age, respectively. All had finished chemotherapy treatment.

For the study's primary endpoint, prevention of greater than a 10 percent reduction in left ventricular ejection fraction at six months, researchers found no significant difference between the carvedilol and placebo groups, 14.5 vs. 13.5 percent, respectively.

Overall, declines in ejection fraction were minimal in both groups and were not statistically significant (from baseline to 24 weeks the average drop in ejection fraction was 65.2 to 63.9 percent in the placebo group and 64.8 to 63.9 percent in the carvedilol group).

Secondary outcomes included carvedilol's effects on two biomarkers, troponin I and B-type natriuretic peptide (BNP), and diastolic dysfunction. Of the 65 (33.8 percent) patients with higher plasma levels of troponin I that are known to be suggestive of heart damage, many more were in the placebo group — 41.6 percent vs. 26 percent. There was no difference in levels of BNP. While not significant, patients in the placebo group tended to have enlarged hearts, compared to patients in the carvedilol group.

Avila said this could indicate that carvedilol may help prevent remodeling or changes in the structure of the heart. According to Avila, the reason why patients taking carvedilol had lower troponin levels, but no differences in changes in ejection fraction, is difficult to explain. She noted that the six-month follow-up may not have been sufficient to see changes in heart function. In addition, any heart damage may not have been severe enough to lead to heart failure. There was only one case of overt heart failure with reduced ejection fraction, which was in the placebo group.

"Previous studies have shown that higher troponin levels can predict cardiovascular events and so we could imagine that carvedilol may be able to prevent these events, but we did not see this finding in our study," she said, adding that she and her team will continue to follow these patients and report data at one and two years.

In the meantime, researchers did find the prevalence of cardiotoxicity in this study to be lower than in previously reported data from other studies — a finding that could be attributed to lower doses of anthracyclines and lower overall cardiovascular risk in the study population. It could be that the beneficial effect of carvedilol might be more pronounced among higher risk patients, Avila said.

In recent years, lower doses of anthracyclines are used to help reduce the risk of heart damage from treatment.

## ACC2018特集

[News01]

気候変動は心筋梗塞リスクを上昇させる可能性がある

[News02]

炎症性腸疾患はMIリスクを上昇させる

[News03]

前向きな態度は狭心症患者の転帰を改善する

[News04]

アリロクマブは急性冠症候群後の心血管イベントを軽減する

[News05]

着型自動除細動器は全死亡を減らすが突然死には影響しない

[News06]

心不全患者にとってインフルエンザワクチンは有益である

[News07]

音楽は運動負荷試験中の運動時間を増加させる

[News08]

がん治療は心不全リスクを上昇させる

[News09]

遺伝子型解析はPCI後の薬物選択において有益である

[News10]

3種の低用量内服は高血圧管理に成功した

[News11]

ACSにおけるスタチンのローディングドーズ投与は臨床イベントリスクを減少させない

[News12]

卵円孔閉鎖患者においてデバイスが転帰を改善する

[News13]

タビガトランは非心臓手術後の心筋障害を軽減する

[News14]

短期抗血小板薬2剤併用療法はMIリスクを上昇させる

[News15]

薬剤が第Ⅹa因子阻害効果をリバースする

[News16]

Canakinumabは糖尿病への進行を予防しない

[News17]

MI後のチカグレロル使用の安全性はクロピドグレルと同等である

[News18]

積極的なモニタリングはAFibの診断率を3倍に上昇させる

[News19]

化学療法による心毒性の軽減

[News20]

カルベジロールは乳がん女性の心臓を保護する