prostacyclin analogue, endothelin receptor antagonist, phosphodieste-
rase 5 inhibitor) from 2012 to 2013. Results: After 1 year of oral triple
combination therapy WHO-FC improved from III to II in all three
patients and 6 min walking test improved from 273 ± 58 to 553 ± 31
(P < 0.05) and mean pulmonary arterial pressure decreased from 52.7 ±
9.5 to 31 ± 6.2 mmHg (P = 0.05) and cardiac index increased from
1.5 ± 0.2 to 2.82 ± 0.17 mmHg (P < 0.001). All three patients were
tolerable with triple upfront combination therapy and had no severe side
effect. Conclusions: Oral triple upfront combination therapy improved
symptoms, exercise capacity and hemodynamics for the patients with
severe I/HPAH in long-term without severe adverse effect.


Combination therapy of bosentan and ambrisentan for
portopulmonary hypertension
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Endothelin receptor antagonists (ERAs) such as bosentan and
ambrisentan are principal medicines in the treatment of pulmonary
arterial hypertension (PAH). On the other hand, the adverse effects are
not uncommon such as liver dysfunction and peripheral edema. These
side effects are often intolerable for patients and hinder administration
of sufficient amount of ERA. In this report, we present a case of a 56-
year-old man with liver cirrhosis due to non-alcoholic steatohepatitis.
He was referred to our hospital complaining of progressive dyspnea on
effort equivalent to WHO FC III. His mean pulmonary artery pressure
(mPAP) was 62 mmHg and peak VO2 was 10.9 ml/kg/min. He was
diagnosed as having portopulmonary hypertension (PoPH). Tadalafil,
bosentan and beraprost were introduced respectively, and his mPAP
ameliorated to 54 mmHg. However, he was intolerant of increasing
bosentan more than 125 mg, because of worsening liver dysfunction,
while a full dose of ambrisentan was hard to use, as he easily got
edematous with various drugs. Finally, we administrated a combination
of moderate dose of bosentan (125 mg) and ambrisentan (25 mg).
Three months after administration of both drugs, his mPAP was reduced
to 42 mmHg, and peak VO2 was improved from 14.7 to 17.8 ml/kg/min,
with no significant adverse effect of each drugs. To our knowledge, this
is the first case report in which a combination therapy of bosentan and
ambrisentan was practically tried to the patient of PAH, and satisfactory
result was obtained. In this report, we will try to discuss the efficacy of
combination therapy of bosentan and ambrisentan, in terms of cross-
talk of endothelin receptors, based on relevant literatures.


Experience in combination therapy for portopulmonary
hypertension in the young with intravenous epoprostenol
and endothelin receptor antagonists
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Background: Portopulmonary hypertension (PoPH) is an uncom-
mon but devastating complication of liver disease. There is no
established medical therapy for PoPH and the condition adversely
affects the outcome of liver transplantation. The prognosis of PoPH in
the young is still very poor even in the recent era. Methods: We
retrospectively reviewed seven pediatric patients with PoPH who were
treated with different combinations of vasodilators. Expression of
endothelin-1 and its receptors in the postmortem lung specimens were
analyzed. Results: Primary diagnoses for liver disease were congenital
biliary atresia in 5, extrahepatic portal vein atresia in one and patent
ductus venosus in the other. The median age at diagnosis was 14 years
old. The onset of PoPH was syncpe, dyspnea on exercise and abnormal
electrocardiogram. The mean pulmonary arterial pressure was
49 mmHg and pulmonary vascular resistance index was 11.2 wood
units–m² at the time of diagnosis. Cardiac catheterization revealed no
acute response to oxygen, nitric oxide, sildenafil whereas a little response
to intravenous epoprostenol (IV-PGI2). IV-PGI2 was adminis-
trated in four patients and had chronic effect on hemodynamics. Oral
endothelin receptor antagonists (ERA: bosentan or ambrisentan) were
administered in five and there was no evidence of drug-related
liver injury. Three patients died and liver transplantation was
performed in three. Immunohistochemical staining for the endothelin
system revealed increased expression of ET-B receptor in the pulmo-


Background: Right heart catheterization (RHC) is the invasive but
the gold standard examination for assessing pulmonary arterial
pressure (PAP). Thus, pulmonary hypertension (PH) is usually predict-
ed by using echocardiographic parameters. Regional deformation of
the left ventricular (LV) wall detected by two-dimensional speckle-tracking
echocardiography is evidently useful for detecting myocardial ischemia,
viability and LV function, but its significance of right ventricle (RV) has
not been fully elucidated. We investigated the ability of peak systolic
strain (PSS) and the post systolic strain index (PSI) of the RV free wall
determined by speckle-tracking echocardiography to predict PH.
Methods: Thirty-six images (27 images from patients with PH; nine
from patients with connective tissue diseases without PH) obtained by
speckle-tracking echocardiography were analysed. PSS and PSI at the
basal and mid-RV free wall were calculated and averaged. We
investigated the relationship of echocardiographic parameters of
pressure/volume overload in RV including RV end-diastolic diameter
(RVDD) and the pressure gradient calculated from the velocity of
tricuspid valve regurgitation (TRPG) with mean PAP (MPAP) measured
by RHC. Results: PSS, PSI, RVDD and TRPG were significantly correlated
with MPAP. Multivariate logistic analysis identified PSS as an indepen-
dent predictor of MPAP ≥ 35 mmHg (odds ratio, 1.62; 95% confidence


Peak systolic strain at right ventricular free wall determined by
two-dimensional speckle-tracking echocardiography is an
independent predictor for pulmonary hypertension
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