Pharmacologic Augmentation in SPECT & SPECT/CT in detecting viable myocardium

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Nitrates

1. Increase myocardial blood flow to hypoperfused myocardial segments by dilating the stenotic lumen
2. Selectively relax the epicardial (conductance) vessels, thereby facilitating flow through collateral channels to zones of myocardial ischemia
3. Decrease LV preload and afterload, thereby decrease the subendocardial compression forces and improving subendocardial perfusion
N-13 ammonia PET study:
Effect of transdermal nitroglycerin on global and regional myocardial perfusion in patients with angiographically proven CAD


• Subjects: 20 pts (age 30-79 yrs) with chronic stable angina responsive to sublingual nitroglycerin

• Double-blind randomized placebo control study:
20 patients were randomly allocated to receive a precordial skin patch containing either nitroglycerin (Nitro-Dur 0.4 mg/h; n=10) or placebo (n=10)
Glucose metabolism

Rest perfusion

Stress perfusion

Apical Infarction

Posterolateral Ischemia
Percent change in regional myocardial perfusion from baseline to 3 hours postpatch for both "nonischemic" and "ischemic" zones: Preferential enhancement of flow to the ischemic zones with nitroglycerin

NTG: nitroglycerin
P: placebo
In summary,

this study shows that the application of topical nitroglycerin appears to exert changes in myocardial perfusion by preferential distribution of flow to areas of myocardial ischemia with little or no significant change in either total myocardial perfusion or cardiac work.
Nitrate Administration Increases Blood Flow in Dysfunctional but Viable Myocardium, Leading to Improved Assessment of Myocardial Viability: A PET Study

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Consecutive 25 patients (all men; mean age 61±10 yr) with chronic ischemic LV dysfunction (LVEF < 45%) were prospectively included.

Patients with unstable angina, recent MI (< 3 mo), or heart failure requiring hospitalization were excluded.

N-13 ammonia PET was used to quantitatively assess blood flow (at rest and after nitrate administration), and F-18 FDG PET was used to detect viable myocardium.
NTG increased myocardial blood flow in viable myocardium, whereas blood flow remained unchanged in nonviable myocardium.
According to ROC curve analysis, a ratio of 1.1 for N-13 ammonia-NTG to N-13 ammonia baseline was the optimal cutoff value for detection of segmental viability, with an AUC of 0.92±0.030.
CONCLUSION

Nitrate-enhanced $^{13}$N-ammonia PET increased myocardial blood flow in viable myocardium, whereas blood flow remained unchanged in nonviable myocardium. The ratio of nitrate-enhanced flow to resting flow was the best predictor of viability, yielding a sensitivity of 82% and a specificity of 100%.
viability

a shift toward normal of at least two grades or complete normalization of a resting image compared with the initial exercise image
For nitrate imaging, criteria of $^{99m}$Tc sestamibi injection
1. Systolic BP dropping $>20$ mmHg
2. Systolic BP $<90$ mmHg
3. None of 1 or 2, 15 min after the start of infusion, and the infusion was maintained for a further 2 min

- Asynergic segments were defined viable if an activity increase $>10\%$ is registered in nitrate SPECT compared to baseline imaging.
- Conversely, viability was excluded in the case of nitrate-induced decrease $>10\%$.
- In the segments with a nitrate-induced activity change between 6-10\% of baseline activity, viability was considered to be present if activity in nitrate SPECT was $>65\%$. 

Sciagra et al.
# Prognostic Utility of Nitrate Imaging

## Table 1  Baseline data of the prognostic studies

<table>
<thead>
<tr>
<th>Author</th>
<th>Patients</th>
<th>Prior MI (%)</th>
<th>LV EF (mean, %)</th>
<th>Imaging agent</th>
<th>Nitrate administration</th>
<th>Imaging protocol</th>
<th>Viability criterion of dysfunctional segment</th>
<th>Treatment (Rev, %)</th>
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<tbody>
<tr>
<td>Basu et al. [20]</td>
<td>100</td>
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<td>46</td>
<td>$^{201}$TI</td>
<td>Sublingual</td>
<td>Stress/nitrate</td>
<td>Reversible defects</td>
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LVEF, left ventricular ejection fraction; MI, myocardial infarction; Rev, revascularization.  
*Patients with early revascularization were censored.
The majority of the patients recruited in these studies had a history of prior MI (75–100%) and LVEF ranged from an average of 25–46%.

Most studies (eight out of nine) used 99mTc-sestamibi as an imaging agent, and baseline-nitrate imaging was the most favored imaging protocol (six out of nine).

As to the modality of nitrate administration, sublingual or i.v. infusion was similarly used.

Myocardial viability of dysfunctional segments was determined by the post-nitrate uptake, nitrate-augmented increase uptake, or both.

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LVEF, left ventricular ejection fraction; MI, myocardial infarction; Rev, revascularization.

*Patients with early revascularization were censored.
Seven studies investigated the predictors of event-free survival using univariate and/or multivariate regression analysis.

They consistently showed the close relationship between myocardial viability evaluated by nitrate-augmented MPI and the occurrence of cardiac events.
Patients with more viable myocardium would have better outcome if they underwent coronary revascularization than pts treated medically.
• In patients who received medical treatment after evaluation of myocardial viability, the event-free survival was lower in those with viability at nitrate imaging compared with those without.
Diagnostic Performance of Nitrate Imaging

- Dysfunctional segments with < 55% tetrofosmin uptake at baseline or nitrate imaging, or >10% increase after nitrate, were considered viable.
- They demonstrated the concordance between tetrofosmin SPECT and FDG PET in differentiating viable and necrotic myocardium was in 82% segments (k=0.53), and the sensitivity and specificity of nitrate imaging were 81 and 86% in comparison with PET.
By use of a receiver operating characteristic (ROC)–derived cutoff value of 63% for regional Tc-99m tetrofosmin uptake, post-nitrate imaging showed a higher global accuracy, with a significantly greater area under the ROC curve, as compared with resting imaging.
Nitrate and Viability

Tc-99m-sestamibi SPECT for myocardial viability
: Pooled data

Without Nitrate (n=308 from 13 studies)
sensitivity 79%, specificity 58%

With Nitrate (n=180 from 7 studies)
sensitivity 86%, specificity 83%
65/M

CC: for evaluation of myocardial viability

PH: DM on medication

SH: alcohol – 20년 전 quit (social)
smoking - 20년 전 quit (20 PYS)

FH: N-S

PI: exertional dyspnea for years
diffuse narrowing of LAD on CAG
Nitrate Tc-99m tetrofosmin myocardial perfusion SPECT

TID Ratio

1.03
Severity Polar Map
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<td>EF</td>
<td>51% (R0)</td>
<td>41% (R0)</td>
</tr>
<tr>
<td>EDV</td>
<td>201 ml</td>
<td>207 ml</td>
</tr>
<tr>
<td>ESV</td>
<td>99 ml</td>
<td>122 ml</td>
</tr>
<tr>
<td>SV</td>
<td>102 ml</td>
<td>85 ml</td>
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<tr>
<td>Mass</td>
<td>194 gm</td>
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Estimated % Thickening:

- > 40%
- 25% => 40%
- 10% => 25%
- 0% => 10%
- -10% => 0%
- < -10%
S, R: perfusion on stress & rest, Tc-99m tetrofosmin SPECT
M: glucose metabolism, F-18 FDG PET
S, R: perfusion on stress & rest, Tc-99m tetrofosmin SPECT
M: glucose metabolism, F-18 FDG PET
Conclusion

Nonviable myocardium

Nontransmural infarction ~ 50%

Inducible ischemia (viable myocardium)
Delayed Enhancement, CMR

Transmural

DE-CMR
Sensitivity 99%, specificity 94%
SPECT
Sensitivity 86%, specificity 68%

Subendocardial

# Prediction of Functional Recovery by CMR

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<th>Transmurality threshold</th>
<th>&gt;50%</th>
<th>&gt;25%</th>
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<tr>
<td>Negative predictive value</td>
<td>92%</td>
<td>79%</td>
</tr>
<tr>
<td>Positive predictive value</td>
<td>66%</td>
<td>71%</td>
</tr>
</tbody>
</table>

Prediction of Functional Recovery Using Quantitation of Thallium-201 vs Technetium-99m Sestamibi Activities

\[ r = 0.85 \]
\[ p < 0.001 \]

Inducible Ischemia

= most specific finding for functional recovery

Circulation 1998; 98:501–8
Functional Recovery after Revascularization

S  R  M
30% 96% 0%
Thank you for your attention