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Original Article

Ischemic Modified Albumin (IMA) as a Novel Marker for Ischemic Heart Disease and Surrogate Marker for Other High Oxidative -Ischemic Conditions

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ABSTRACT

Aims and Objectives: To find out if ischemia modified albumin can be a novel marker in ischemic heart disease. **Materials and methods:** Retrospective chart-review of chest pain patients who were evaluated in the emergency departments in 2006 and 2007. **Results:** Total of 400 patients presented with chest pain and subsequently were evaluated in the Emergency department at two major emergency departments associated with the teaching hospital associated Mercy Catholic Medical Center; few patients were excluded due to unavailability of complete data and follow-up visit in next six months. Thus, finally 351 patients met criteria for final analysis. Primary endpoints included the cardiac events and secondary outcomes were course in the hospital, days of hospitalization, interventions done in the hospital, disposition from the hospital, and readmission within next six months. Sensitivity and specificity of ischemia modified albumin (IMA) test was 80% and 50% respectively and positive predictive value and negative predictive values were 17% and 88% respectively. There were no further differences in cardiac events or interventions in higher ischemia modified albumin (IMA) group as compared to troponin (cTnT) (p=0.5). People with higher ischemia modified albumin (IMA) showed longer hospitalization days (p=0.025), needing nursing home or skilled nursing facility on discharge due to high discharge needs (p=0.0001) and had more readmissions as compared to troponin (p=0.02). However, Higher ischemia modified albumin (IMA) did not predict more cardiovascular events during hospital stay, rather troponin (cTnT) test predicted arrhythmia more than ischemia modified albumin (IMA) test (p=0.0001). **Conclusion:** Ischemia-modified albumin may be utilized as a novel marker of ischemia to rule out acute coronary syndrome along with troponin and electrocardiogram in the emergency departments. This test may also have short and long-term prognostic significances and may even be used as a surrogate marker in stroke, sepsis and thrombo-embolic diseases once these people need admission to the hospital.
Key words: Acute Coronary Syndrome, Ischemia Modified Albumin, Ischemic Heart Disease, Prognosis.

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INTRODUCTION

Acute myocardial infarction and ischemic cardiac conditions are one of the most difficult situations emergency physician has to deal in view of exercising clinical decisions regarding admission or discharge from the emergency department. Studies over past couple of years have shown that ischemia-modified albumin (IMA) is a biomarker of ischemia in several clinical scenarios and it is highly sensitive for the diagnosis of myocardial ischemia in patients presenting with symptoms of acute chest pain.[1] It has been shown to increase in presence of myocardial ischemia associated with percutaneous coronary intervention (PCI) and is also high in conditions of high oxidative stress.[2] However, little is known about its ability to diagnose ischemic cardiac conditions accurately and differentiate it from other ischemic conditions or predict future adverse outcomes in patients with positive markers presenting to the hospital. Emergency physicians utilize ischemia-modified albumin (IMA) for the diagnosis of myocardial ischemia as it improves the usefulness of standard cardiac biomarkers for the diagnosis of myocardial ischemia in the emergency department setting.[3]

Cardiac ischemia is the most common mechanisms underlying acute coronary syndrome (ACS).[4,5] Ischemia modified albumin (IMA) is produced as a result of tissue ischemia and is present in blood in easily detectable concentrations.[6,7] We thus decided to find out the utility of ischemia modified albumin (IMA) in patients suspected of acute coronary syndrome, its role to predict adverse outcome with high IMA and thus short and long-term prognostic significance of high ischemia modified albumin (IMA) during hospitalizations and for six months after discharge as this has not been studied previously. Since the relationship between ischemia modified albumin (IMA) and other conditions like stroke, inflammations etc. which could be grouped as non-cardiac ischemic events has not been clearly understood,[7] we also analyzed relationship of the rise in IMA in other conditions as described below (stroke, sepsis, seizure, etc.).

MATERIALS AND METHODS

Total of 400 patients who presented with chest pain and subsequently were evaluated for ischemic heart disease were taken into the study. Retrospective chart reviews of these patients were done during 2006 and 2007. Few patients did not follow up and had inadequate data, thus 351 patients fulfilled criteria for final analysis and others were excluded. Local institutional review board (IRB) at Mercy Fitzgerald Hospital approved the study in January 2008 as per the protocol of the institution for any study.

Inclusion criteria included - All patients who were evaluated in the emergency department for coronary artery disease were included in the study. An exclusion criterion was frank ST elevation at the time of presentation. Data collections were done at Mercy Fitzgerald Hospital and final diagnosis was analyzed with reference to the utility of ischemic modified albumin (IMA) and troponin (TnT) as a cardiac biomarker and their prognostic significance. ST-segment elevation myocardial infarction

(STEMI) was diagnosed if there was ST segment elevation >0.1mv in 2 or more contiguous leads with cardiac troponin (cTnT) >0.05ng/ml; non-ST-segment elevation myocardial infarction (NSTEMI) was diagnosed if EKG did not show ST-segment elevation and troponin (cTnT) was >0.05ng/ml. Patients were classified as atypical chest pain when i) a non-cardiac mechanism was confirmed as the cause of chest pain ii) troponin (cTnT) results were negative on serial sampling (three samples six hours apart) iii) neither Electrocardiogram (EKG) changes nor evidence of coronary artery disease were present. Other conditions contributing rise in ischemic modified albumin (IMA) were also analyzed on the basis of final discharge diagnosis. Primary outcome measures were cardiac events and secondary outcomes included- need of cardiac interventions, days of hospitalizations, course in the hospital including arrhythmias and deaths, disposition from hospital, readmission in next six months.

Statistical analysis

Statistical software SPSS version 16.0 for windows (SPSS, Chicago, IL, USA) and analyse-it for Microsoft Excel version 2.09 (www.analyseit.com) were used for analysis. Receivers operating characteristic (ROC) curves were plotted for ischemia-modified albumin (IMA). Positive troponin value was considered >0.05ng/ml and IMA >95 IU/L. Sensitivity, Specificity, Positive and Negative predictive values calculated. Chi Square and two tailed students *t*-test were used where required. Significant levels were taken as $p \leq 0.05$.

RESULTS

Final analysis was done in 351 subjects who fulfilled requirements for analysis. Males and females were 173 (49.3%) and 178 (50.7%) respectively. African Americans 189 (53.8%) was the majority followed by Caucasians 143(40.7%), Hispanic 15(4.3%), and Asian 4(1.1%) populations. The area under the ROC curve for ischemia-modified albumin (IMA) was 0.753±SE0.98 (95% CI 0.56- 0.945). At optimum level of 95.5 IU/L, sensitivity and specificity was 80% and 50% respectively. Similarly positive and negative predictive values calculated for ischemia modified albumin (IMA) alone were 18% and 88% respectively. Age, sex, race and previous interventions including cardiac catherizations with or without stents and coronary artery bypass surgery did not have influence in ischemia modified albumin (IMA) values. Highest values of ischemia-modified albumin (IMA) were found in non-cardiac conditions (Table 1) like sepsis (mean±SD) 148±17.68, Cholecystitis 118±23.92,venous thromboembolism 112±13.87,Seizure 111±0.01, etc. Five people with borderline ST elevation at presentation were finally considered to have definite ST-elevation myocardial infarction showed even less ischemia modified albumin (IMA) values possibly because the ischemia might have already occurred and infarction might have ensued. Rise in ischemia-modified albumin (IMA) alone did not influence cardiovascular outcomes including need of interventions like stress tests, cardiac catherizations, stenting and coronary artery bypass surgery. People with higher troponins showed more arrhythmias than higher IMAs (p=0.000) (table2). Death was higher in people with high ischemia modified albumin (IMA) and Troponin T (TnT) level (p=0.000). People with higher ischemia modified albumin (IMA) showed more hospitalization days (p=0.025) and had more readmissions in next six months (p=0.02). They also require nursing homes or skilled nursing facility on discharge from the hospital due to higher disability and dispositions needs like rehabilitation and safety.

DISCUSSION

Our study for the first time has highlighted the novel biomarker has many potential utilities including diagnosing many conditions , differentiating ischemic heart disease from non-ischemic and even prognostic value. High levels of ischemia modified albumin (IMA) clearly predicted adverse outcomes in patients namely increasing hospitalization days, requiring nursing home and skilled nursing facility for safe discharges, more morbidity and mortality and even poorer prognosis even after six months as they had high readmission rates. These findings complement[7-9] and expand the findings in the earlier study by Consumer-Sanchez *et al*[10] for predicting short-term prognosis and 1-year mortality for the first time and the study by Sinha *et al*[6] that people with high ischemia modified albumin (IMA) should be followed up carefully during hospitalization and post-discharge.

There have been very little studies assessing the prognostic value of ischemia-modified albumin (IMA). Recently Consuegra-Sanchez *et al*[10] prospectively studied 207 patients presenting to emergency department with chest pain within 3 hours of onset of pain. Ischemia modified albumin (IMA) was obtained on admission. 30-day combined end points including cardiac death, myocardial infarction, recurrent angina and 1-year all-cause mortality was evaluated. People with higher IMA above 93.3U/ml showed higher short-term end points (20.4%Vs 9.6%) and higher 1-year mortality rate (11.7% vs 3.8%) that High ischemia modified albumin (IMA) was independent predictor of both of these outcomes. Meta-analysis done by Peacock *et al*[11] had also shown that triple negative prediction test of ischemia modified albumin (IMA), electrocardiogram and troponin measured within 3 hours of chest pain had not only have high negative predictive value for excluding acute coronary syndrome but also was cost-effective and did have better 30-day and 6-month outcomes.

Collinson *et al*[4] reported outcomes in 446 patients at six months with low risk acute chest pain. In this study people with known coronary artery disease, significant electrocardiogram changes and unstable angina were excluded; the percentage of events was only 3.8% with 6 cardiac deaths. Relative risk of events was higher in those with high Troponin (cTnT) and ischemia modified albumin (IMA) (21%) versus negative ischemia modifies albumin (IMA) plus troponin (cTnT) (1.5%) but neither ischemia modified albumin (IMA) nor troponin (cTnT) alone were predictive of events as in Peacock's meta-analysis.[11]

Dusek *et al*[12] reported in 60 patients with stable angina pectoris who underwent elective percutaneous intervention (PCI) that a median follow up of 46 months, people with higher ischemia modified albumin (IMA) (>130 U/L) was found to be associated with higher target vessel revascularization rate in the univariate analysis though there were no death or myocardial infarctions noted. This shows ischemia modified albumin (IMA) may be a useful marker to predict further need of re-intervention after percutaneous intervention or revascularization (PCI).

However, Worster *et al*[9] evaluated 189 patients with chest pain within 6 hours of onset of symptoms. Using cutoff ischemia modified albumin (IMA) of 80 U/ml, they documented 24 serious adverse outcomes at 72 hours including death, myocardial infarction (MI), congestive heart failure (CHF), and refractory chest pain. They had maximum sensitivity of 92.3% and specificity of 24.3% suggesting ischemia-modified albumin (IMA) to be a poor predictor of serious cardiac events in the short term.

The long-term prognostic role of ischemia modified albumin (IMA) was evaluated by Sharma *et al*[13] in a sample of 114 renal transplant candidates. They found that ischemia modified albumin (IMA) and troponin (cTnT) combined not alone were independent predictors of death. Ischemia modified albumin (IMA) above 95 U/ml predicted long-term mortality with a sensitivity of 75% and a specificity of 72%.

Ischemia modified albumin (IMA) test does predict early about the cardiac ischemia.[14-16] and is a good prognostic marker in chronic ischemic heart failure [16] and Coronary artery bypass graft surgery (CABG).[17] This is positive in a variety of conditions giving rise to tissue ischemia.[18,19] Our study highlights the importance of evaluating patient populations for testing as more false positive elevations in ischemia modified al-

Table 1: Final Diagnosis in the Study Population

Diagnosis Atypical CP N=133 (39.3%)	IMA (Mean±SD) 95.19±11.09	TnT (Mean±SD) 0.03±0.03
COPD Asthma N=42(12%)	95.67±11.23	0.0119±0.0U)
Coronary Artery Disease N=40 (11.4%)	97.93±16.10	0.056±0.174
GERD Gastritis N=35 (10%)	101.11±19.41	0.034±0.42
CI T N- 3 3 (9.4%)	103.58 ± 115.84	0.99±5.46
Pneumonia N=16 (4.6%)	97.31±17.53	0.0164±0.024
Cocain abuse N=7(2%)	95.294-17.9	0.011-60.003
Anemia N=6(1.7%)	93.33±16.33	0.03±0.04
TIA Stroke N=5(1.4%)	99.2±10.13	0.01±0.00
DVT PE N=5(1.4%)	112±13.37	0.03±0.044
STEM E N=5(1.4%)	93.40±3.264	0.324±1.65
Cholelithiasistholecystitis N=5(1.4%)	113±23.92	0.01±0.00
Sepsis N=2(0.6%)	143±17.673	0.013±0.002
Takotsubo N=2(0.6%)	96.5±6.36	0.13±0.24
DC 42N-2(0.6%)	94-1.41	0.06±0.07
Rhabdomyolysis N=2(0.6%)	90z5.65	0.01±0.00
SW N-2(0.6%)	34±5.65	0.067±0.017
Pancreatitis N=1(0.3%)	100	0.21
Perirarditic N=1(0 3%)	103	001
Accelerated HTN N=1(0.3%)	95	0.01
Seizure N=1(0.3%)	111±0.01	0.01±0.00

Table 2: Final results (NH-nursing home, SNF-Skilled Nursing Facility, NS-non-significant, CTA- CT angiography)

Outcome Variables		Number (% of total)	IMA (mean±SD)	TnT (mean±SD)	P value (significant <0.05)
Course / Arrythmia	Yes	18(5.1%)	95.83±11.39	0.26±0.89	0.000
No	328(93.4%)	97.95±14.76	0.04±0.16	NS	
Death		5 (1.4%)	104.4±28.64	6.32±14.03	0.000
Hospitalization (Days)	< 5 days	295 (84%)	97.02±13.66	0.15±1.83	0.025
	5-9 days	44(12.5%)	103.36±16.55	0.11±0.57	0.025
	>10 days	12(3.4%)	100.50±28.24	0.06±0.08	0.025
Disposition	Home	307(87.7%)	96.13±12.49	0.04±0.17	NS
	NH/SNF	38(10.9%)	111.95±21.53	0.14±0.61	0.000
Readmission (in next 6 months)	Yes	81(23.1%)	101.20±SE1.89	0.08±SE0.05	0.02
	No	270(76.9%)	96.96±SE0.85	0.16±SE0.12	0.7
Interventions	No	219(69.4%)	97.97±15.84	0.18±2.13	0.5
	Cath	29(8.3%)	94.48±8.65	0.07±0.12	NS
	Stress	47(13.4%)	98.98±14.94	0.10±0.55	0.5
	Echo	53(15.1%)	98.85±13.17	0.02±0.02	0.5
	CT A (angio)	2(0.6%)	104.5±9.19	0.10±0.13	0.5

bumin was found in different conditions while evaluating for ischemic heart disease including cholecystitis, pericarditis, pancreatitis, stroke, seizures and pulmonary thromboembolic phenomena.[20,21,22,23,24,25,26] Ischemia modified albumin may thus be used as a surrogate marker in those conditions but more prospective detailed studies are required in the future. It can be utilized as a rule out test rather than rule in test due to high negative predictive value along with electrocardiogram (EKG) and troponin (cTnT) to increase sensitivity and specificity. It alone did not have clear edge over troponin (cTnT) in predicting cardiac arrhythmias, heart failure or need of interventions, probably because troponins are more specific and indicate injury and ischemia modified albumin (IMA) only early ischemia.[27] Our study seems in concordance with all the other studies available in the literature and shows similar role of ischemia-modified albumin (IMA).

Study limitations

Our study was retrospective and was conducted in a single teaching center, which may limit the generalizability of the results. In our study, time of onset of symptoms was also variable from few minutes to hours; this might need caution in interpretation to general population. However, this is the first report of its kind which not only shows its definite usefulness in utilizing it as a novel biomarker in cardiac ischemia and other oxidative conditions but also prognostic implications of high ischemia modified albumin (IMA) in other conditions, namely to find who needs more hospitalization days, will need better dispositions along with their poor outcomes in next six months. Nonetheless, this has yet to be confirmed with randomized large-scale randomized trials before larger applications into the general population.

CONCLUSION

There were no statistical significant differences in predicting cardiovascular endpoints by ischemia modified albumin (IMA) test as compared to troponin (cTnT) alone. As ischemia modified albumin had more negative predictive value, it could be utilized in combination with electrocardiogram and troponin in discharging patients from emergency departments. Troponin did predict significant arrhythmias than ischemia modified albumin (IMA) but people with higher ischemia modified albumin (IMA) test did show more hospitalization days, needing skilled nursing facility on discharge and more readmissions as compared to troponin that was statistically significant. It has also shown its potential role as a surrogate marker in predicting ischemic stroke and severity of sepsis. However more prospective and elaborate studies are required before it can be utilized in any other areas as a surrogate marker. Finally, high ischemia modified albumin (IMA) may help identifying patients with short and long term poor prognosis other than only diagnosis of ischemic heart disease. Thus we recommend that people with high ischemia modified albumin (IMA) on arrival to the emergency department should be evaluated and followed up carefully even if electrocardiogram (EKG) and troponin (cTnT) are negative for ischemic heart disease for possible other etiologies of high oxidative stress and potential for long term poor outcomes.

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CONFLICT OF INTEREST

The authors are declared no conflict of interest.

ABBREVIATION USED

ACS: Acute coronary syndrome, **ED:** Emergency Department, **EKG:** Electrocardiogram, **CTA:** CT angiogram, **IMA:** Ischemia modified albumin, **STEMI:** ST elevated myocardial infarction; **NSTEMI:** Non-ST elevated myocardial infarction.

REFERENCES

1. Apple FS, Wu AHB, Mair J, *et al.* Future biomarkers for detection of ischemia and risk stratification in acute coronary syndrome. Clinical chemistry .2005;51(5):810-24.
2. Melanson SF, Tanasijevic MJ. Laboratory diagnosis of acute myocardial injury. Cardiovascular pathology. 2005;14:156-61.
3. Anwaruddin S, Januzzi Jr JL, Baggish AL, Lewandrowski L, *et al.* Ischemia modified albumin improves the usefulness of standard cardiac biomarkers for the diagnosis of myocardial ischemia in the emergency department setting. Am J Clin Pathol. 2005;123(1):140-145.
4. Collinson PO, Gaze DC, Bainbridge K, Morris F, Morris B, Price A, Goodacre S. Utility of admission cardiac troponin and ischemia modified albumin measurements for rapid evaluation and rule out of suspected acute myocardial infarction in the emergency department. Emerg Med J. 2006;23(4):256-61.
5. Chan MY, Pronovost PJ. Clinical utility of biomarkers in myocardial injury. Current opin Anesthesiol. 2004;17(1):49-55.
6. Sinha MK, Gaze DC, Collinson PO, Kaski JC. Role of ischemia modified albumin, a new biochemical marker of myocardial ischemia in the early diagnosis of acute coronary syndromes. Emerg Med J. 2004;21(1):29-34.
7. Tawalkar SS, Bon-Homme M, Miller JJ, Elin RJ. Ischemia modified albumin, a marker of acute ischemic events: a pilot study. Annals of clinical Laboratory science. 2008;38(2):132-37.
8. Turedi S, Gunduz A, Mentese A, *et al.* The value of ischemia-modified albumin compared with d-Dimer in the diagnosis of pulmonary embolism. Respiratory research 2008;9(1):49 Downloaded from http://respiratory-research.com/content/9/1/49
9. Worster A, Devereaux PJ, Heels-Ansdell D, Guyatt GH, Opie J, Mookadam F, Hill SA. Capability of ischemia-modified albumin to predict serious outcomes in the short term among patients with potential acute coronary syndrome. CMAJ. 2005;172(13):1685-90.
10. Consuegra-sanchez L, Bouzas-Mosquera A, Sinha MK, Collinson PO, Gaze DC, Kaski JC. Ischemia-modified albumin predicts short-term outcome and 1-year mortality in patients attending the emergency department for acute ischemic chest pain. Heart Vessels. 2008;23(3)174-80.
11. Peacock F, Morris DL, Anwaruddin S, *et al.* Meta-analysis of ischemia-modified albumin to rule out acute coronary syndromes in the emergency department. Am Heart J. 2006;152(2):253-62.
12. Dusek J,St'asek J,Tichy M, Bis J, Gregor J, *et al.* Prognostic significance of ischemia modified albumin after percutaneous coronary intervention. Clin Chim Acta 2006;23:256-61.
13. Sharma R, Gaze DC, Pellerin D, Mehta RL, Gregson H, Streather CP, Collinson PO, Brecker SJ. Ischemia modified albumin predicts mortality in ESRD. Am J Kidney Dis. 2006;47(3):493-502.
14. Gaze DC. Ischemia modified albumin: a novel biomarker for the detection of cardiac ischemia. Drug Metab Pharmacokinet. 2009;24(4):333-41.
15. Bhagavan NV, Lai, EM, Rios PA *et al.*"Evaluation of human serum albumin cobalt binding assay for the assessment of myocardial ischemia and myocardial infarction," Clinical Chemistry. 2003;49(4):581–5
16. Ellidag HY, Eren E, Yilmaz N, Cekin Y. Oxidative stress and ischemia-modified albumin in chronic ischemic heart failure. Redox Resp. 2014;19(3):118-23. doi: 10.1179/1351000213Y.0000000083. Epub 2014 Jan 13.
17. Kanko M, Yavuz S, Duman C, Hosten T, Oner E, Berki T. Ischemia-modified albumin use as a prognostic factor in coronary bypass surgery. Journal of Cardiothoraci surgery. 2012(7):3. DOI: 10.1186/1749-8090-7-3
18. Ellidag H, Buller N, Eren E , Abusoglu S, *et al.* Ischemia-Modified Albumin: Could It Be a New Oxidative Stress Biomarker for Colorectal Carcinoma? Gut Liver. 2013;7(6):675–80.
19. Kumar PA, Subramanian K. The role of ischemia modified albumin as a biomarker in patients with chronic liver disease. J Clin Diagn Res. 2016;10(3): BC09-12.
20. Chawla R, Loomba R, Guru D, Loomba V. Ischemia Modified Albumin (IMA) - A Marker of Glycaemic Control and Vascular Complications in Type 2 Diabetes Mellitus. J Clin Diagn Res. 2016;10(3): BC13–BC16.
21. Jena I1, Nayak SR1, Behera S1, Singh B1, Ray S1, Jena D2, Singh S3, Sahoo SK. Evaluation of ischemia-modified albumin, oxidative stress, and antioxidant status in acute ischemic stroke patients. J Nat Sci Biol Med. 2017;8(1):110-3. doi: 10.4103/0976-9668.198346.
22. Kilic MO, Guldogan CE, Malamir I, Tez M. Ischemia-modified albumin as a predictor of the severity of acute appendicitis. American Journal of Emergency Medicine. 35 2017;35(1):92–5.

23. Ukinc K1, Eminagaoglu S, Ersoz HO, Erem C, Karahan C, Hacihasanoglu AB, Kocak M. A novel indicator of widespread endothelial damage and ischemia in diabetic patients: ischemia-modified albumin. Endocrine. 2009;36(3):425-32. doi: 10.1007/s12020-009-9236-5. Epub 2009 Sep 26.
24. Seshadri Reddy V1, Sethi S, Gupta N, Agrawal P, Chander Siwach R. Significance of Ischemia modified albumin as a simple measure of oxidative stress and its discriminatory ability in diabetic retinopathy: literature review and meta-analysis.Retina.2016Jun;36(6):1049-57.
25. Kaya Z1, Kayrak M2, Gul EE2, Altunbas G2, Toker A3, Kiyici A4, Gunduz M2, Alibaşiç H2, Akilli H2, Aribas A2. The role of ischemia modified albumin in acute pulmonary embolism. Heart Views. 2014;15(4):106-10. doi: 10.4103/1995-705X.151083.
26. Turedi S1, Gunduz A, Mentese A, Topbas M, Karahan SC, Yeniocak S, *et al*. The value of ischemia-modified albumin compared with d-dimer in the diagnosis of pulmonary embolism. Respir Res. 2008;30;9:49. doi: 10.1186/1465-9921-9-49.
27. Sbarouni E1, Georgiadou P, Voudris V. Ischemia modified albumin changes - review and clinical implications. Clin Chem Lab Med. 2011;49(2):177-84. doi: 10.1515/CCLM.2011.037. Epub 2010 Nov 18.

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