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Original Research Article

Effect of metabolic syndrome on treatment outcome of lower urinary tract symptoms in males due to benign prostatic hyperplasia

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ABSTRACT

Lower urinary tract symptoms in males are mostly due to benign prostatic hyperplasia and overactive bladder. Approximately three-fourths of them require medical management with drugs like α_1 blockers and 5-α reductase inhibitors. Metabolic syndrome[MeS] as a comorbidity has been documented with a number of cases of benign prostatic hyperplasia [BPH]. The present study finds MeS as a potential risk factor for BPH and compares the effectiveness of BPH medications among those with and /or without underlying MeS. Patients were evaluated basing on the parameters like biochemical findings and clinical symptoms using IPSS Score, Quality of Life Score, prostate volume using Ultrasound abdomen and pelvis. Our study revealed that, waist circumference, BMI, FBS, Total Cholesterol, HDL cholesterol, LDL cholesterol & HOMA-IR were the significantly associated with the clinical outcome in the MetS +ve patients having BPH. MetS significantly affects the response to medical treatment of BPH as revealed from the IPSS Score, prostate volume and quality of life index. It also emphasizes that MetS evaluation should be an integral part of the standard assessment of male patients with LUTS as well as a new domain in clinical and basic research.

1. Introduction

Most common causes of lower urinary tract symptoms [LUTS] in males are benign prostatic hyperplasia (BPH) and overactive bladder (OAB).In aging males along with the other geriatric health problems there is a gradual rise in the incidence of BPH from the 6^{th} to 9^{th} decades of life and reaches to 80% by 80 years of age. Approximately three-fourths of men with symptoms of LUTS aged more than 50 years require medical management for BPH.[1,2]

The metabolic syndrome (MetS, syndrome X, insulin resistance syndrome) is highly prevalent in adult population. Metabolic syndrome as a comorbidity increases with age and varies from 7.9% to 39% among developing countries in the World[3] and 9.2% to 43.2 (India).[4,5] MeS consists of a constellation of metabolic abnormalities that confer increased risk of cardiovascular disease (CVD) and diabetes mellitus (DM). The Adult Treatment Panel III Criteria is the one used commonly today because it incorporates the key concepts of MetS and relies on routinely available clinical parameters.[6]

Currently, research works on MetS and the chronic prostatic inflammation are providing new insights on the pathophysiology of LUTS symptoms suggestive of BPH. A number of evidences have pointed towards a direct and significant relationship between MetS and BPH/LUTS.[7–9] The severity of lower urinary tract symptoms in patients with BPH and the likelihood of having diabetes are significantly associated.[10] Presence of MetS had a significantly negative impact on the responsiveness to α1-blocker in men with BPH/LUTS.[11–13] Moreover, Finasteride is an efficient 5-α reductase inhibitor shows mild differences in metabolic profile with slight

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amelioration of glucose metabolism regulation.[14,15]

Currently BPH a condition where treatment approach has transformed from exclusively surgical to an effective and primarily medical management with surgical treatment reserved for cases in which initial management has failed.[16] Evidences show that less than 5% of men on medical management had complications with subsequent surgical intervention at the 4-year follow-up.[17] Currently approved drugs for management of moderate to severe LUTS associated with BPH include Alfuzosin, Doxazosin, Silodosin, Tamsulosin and Terazosin [$\alpha_1$blockers], Dutasteride, Finasteride [5-α reductase inhibitors], Oxybutynin, Darifenacin [Anticholinergics] Tadalafil, sildenafil [Phospodiesterase type 5 inhibitors] and mirabegron [selective β_3–adrenergic agonist].[18] The conventional medications used to treat LUTS secondary to BPH fall into two classes of agents: α1blockers and 5-α reductase inhibitors.[19] These agents are used either alone or in combination (larger prostate volumes). LUTS due to BPH are caused by factors like dynamic (factor regulating tone of the prostatic smooth muscle and bladder neck), static (i.e, factor causing enlarged prostatic adenoma followed by mechanical obstruction), and compensatory (hypertrophy and irritability of the detrusor muscle).[20–23]

There have been a number of studies in different countries and population showing the correlations of metabolic syndrome (MeS) and BPH /prostate volume. However, there is paucity of data with regard to MeS as a risk factor for BPH and comparison of effectiveness of BPH medications among those with and /or without underlying MeS in the population where the present study was conducted. Therefore, findings of the present study would give an important insight in managing the public health burden of BPH with underlying MeS. In this context the present study aims, to find the outcome of medical treatment of BPH in patients having metabolic syndrome as a comorbidity.

2. Objectives of the study

2.1. Primary

1. Assessment of risk factors associated with BPH and MetS
2. Evaluation of the impact of MetS on treatment outcome of BPH.

2.2. Secondary

Comparison of anthropometric, biochemical parameters among patients with / without MetS.

3. Materials and Methods

This was a prospective, open labeled, observational study conducted in the Outpatient Department of Urology and Department of Pharmacology of a tertiary care hospital for a duration of 2 years (Jan.2017 to Jan.2019). Institutional Ethics Committee approval was obtained before initiation of the study. Written informed consent in local language from the study subjects was collected prior to their enrolment. 894 adult males diagnosed to be suffering from LUTS secondary to BPH based on their inclusion exclusion criteria [Table 1] were enrolled for the study. According to the NCEP ATP III definition,[24] metabolic syndrome is present if three or more of the following five criteria are met: waist circumference over 40 inches (men) or 35 inches (women), blood pressure over 130/85 mmHg, fasting triglyceride (TG) level over 150 mg/dl, fasting high-density lipoprotein (HDL) cholesterol level less than 40 mg/dl (men) or 50 mg/dl (women) and fasting blood sugar over 100 mg/dl. The enrolled study participants were further stratified into two groups: a group having MeS and a group not having MeS based on NCEP ATP III Guidelines. All the patients irrespective of their metabolic syndrome status were advised either α_1- Blockers or 5 α- Reductase inhibitors or a combination of both basing on their presenting symptoms. Patients with IPSS >8, prostate size <30 g were prescribed α_1- Blockers [Tamsulosin 0.4 mg or Alfuzosin 10 mg). Those having IPSS >8, prostate size >30 g were treated with combination therapy [Tamsulosin 0.4 mg or Alfuzosin10 mg+Dutasteride 0.5 mg].

3.1. Biochemical evaluation

Body weight, height, waist circumference (WC) of study participants was measured. The body mass index (BMI) was then calculated from the weight and height. Fasting glucose, lipid profile was measured using automated methods and commercially available assays. Insulin resistance was determined by the homeostasis model assessment (HOMA-IR) index, calculated as blood glucose (mmol/l−1) × insulin concentration (μIU/ml−1)/22.5.[25] HOMA-IR cut-off of 2.77 was used to recognize patients having insulin resistance.[26,27] The lipid accumulation product (LAP), a useful marker of metabolic risk was calculated using the equation: LAP = (waist circumference in centimeters − 65) × triglycerides (nmol/l).[28,29]

3.2. Efficacy evaluation

Parameters like -Prostate Symptom Score (I-PSS)[30], Quality of Life Score (QOL)[30] and prostatic volume using Ultrasound abdomen and pelvis (USG) were measured at baseline, 4th, 12th, and 24th week. Efficacy of the treatment received was evaluated by improvement in LUTS at 24th week of treatment basing on the changes observed in the above mentioned parameters. During the study period patients were regularly assessed for clinical, biochemical, USG and IPSS changes treatment modified accordingly.

3.3. Statistical analysis

Data were analyzed using Graph-Pad Prism version 6.0. Continuous variables like IPSS, QOL Score, and USG findings were expressed as mean ± SD. Differences among groups were analyzed by an independent t-test or nonparametric Mann–Whitney U-test for continuous variables. Discrete variables were expressed as absolute numbers and percentage, and were compared by Chi-square test/Fisher's exact test.

4. Results

This study was conducted between January 2017 and January 2019**.** Total 894 patients were enrolled during this period. All the study participants were screened for metabolic syndrome initially and further divided into MeS +ve and MeS-ve groups. But at the end of the study, 49 patients were lost to follow-up [LFU]. Therefore of rest 845 patients [MeS +ve (370) and MeS-ve (475)] comprised the study population. Majority (84%) of patients belonged to the age group of 51-75 years with 5% in the age of 40-50 years and 11% in the age of 76-85 years. Anthropometric characteristics like BMI and waist circumference differed significantly among MetS+ and MetS- groups. [Table 2] Similarly both the groups differed significantly with respect to FBG (Fasting blood glucose) and HDL Cholesterol on evaluation of the biochemical variables. [Table 3] Risk factor analysis revealed that, waist circumference >102cm, BMI >25kg/m^2, FBS >110mg/dl, Total Cholesterol >200mg/dl, HDL cholesterol <40md/dl, LDL cholesterol >100mg/dl & HOMA-IR >2.77 were the associated in the MetS +ve patients.[Table 5]

Table 2: Anthropometric characteristics of the Study population

Variable	MetS + ve	MetS - ve	p value
Age	65.05±8.65	64.60±9.4	0.1488
BMI (kg/m^2)	30.37±2.76	24.22±1.93	<0.001**
Waist circumference (cm)	104.01±2.13	89.27±2.27	<0.001**

** p value <0.001 considered significant

Table 3: Biochemical Profile of the Study population

Variable	MetS + ve	MetS - ve	p value
FBG(mmol/l)	7.27±0.20	5.65±0.53	<0.05*
Total Cholesterol (mmol/l)	5.29±0.08	4.91±0.28	0.873
LDL(mmol/l)	2.64±0.03	2.53±0.04	0.753
HDL(mmol/l)	0.67±0.03	1.09±0.05	<0.05*

*p value < 0.05 considered significant

Table 4: Analysis of LAP Score and Insulin resistance of the study population

	MetS + ve	MetS - ve	p-value
Lipid Accumulation Product(LAP) Score	67.29±3.83	35.74±5.02	<0.001**
Serum Insulin(μIU/ml)	17.01±0.34	12.30±0.17	<0.05*
Homeostasis model assessment- insulin resistance(HOMA-IR)	5.49±0.17	2.74±0.32	<0.001**

Analyzed by Independent t-test *p value <0.05, ** p value <0.001 considered significant

Table 6: Impact of MetS on treatment outcome of BPH

	Before T/T		p-value	After T/T		p-value
	MetS +ve	MetS -ve		MetS +ve	MetS -ve	
IPSS Score	21.86	15.91	<0.05	1.44	0.78	0.0283*
QOL Score	4.27	3.24	<0.05	0.84	0.70	0.041*
Prostate Volume(cc)	54.20	28.06	<0.05	24.59	18.77	0.035*

Analyzed by Independent t-test, *p value <0.05 considered significant.

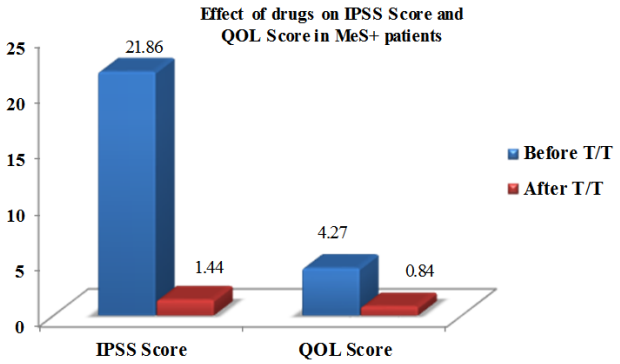

Fig. 1:

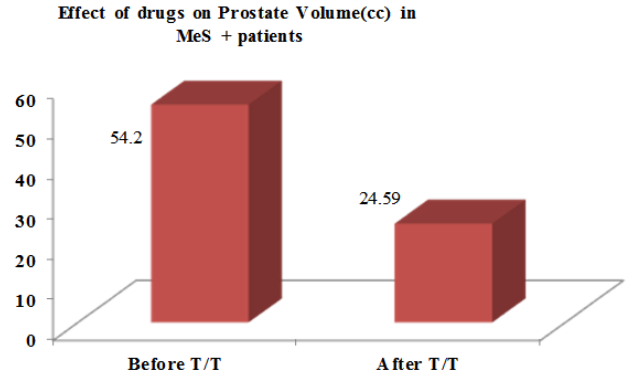

Fig. 2:

Table 1:

	Inclusion Criteria:
1.	Age group 40 – 85 years.
2.	Newly Diagnosed cases of LUTS secondary to BPH who were not on any BPH medication 3 months prior to their enrolment in the study.
	Exclusion criteria:
1.	Old cases of LUTS secondary to BPH.
2.	Evidence or suspicion of prostate cancer.
3.	History of urologic surgery or procedures within 15 days of study entry.
4.	Patients taking alpha blockers as medication
5.	Complications of BPH like chronic kidney disease (CKD), urinary tract infection, chronic prostatitis, bladder stone, severe infection.

Table 5: Risk factors associated with BPH and MetS (MetS +ve vs. MetS –ve)

Risk Factors	Odd's Ratio (95% CI)	p value
Age (≤65 vs. >65 year)	0.66 (0.38 to 1.16)	0.1488
Waist circumference (<102 cm vs. >102 cm)	0.00083(0.0005 to 0.014)	<0.05
BMI (<24.9 vs. > 25 kg/m^2)	0.052(0.02 to 0.13)	<0.05
FBS (<110 mg/dl vs.>110 mg/dl)	0.0011(0.00066 to 0.019)	<0.05
Total Cholesterol (<200 mg/dl vs >200mg/dl)	0.02(0.008 to 0.051)	<0.05
HDL (>40 mg/dl vs <40mg/dl)	0.008(0.0086 to 0.0066)	<0.05
HOMA-IR (<2.77 vs >2.77)	0.002(0.0002 to 0.0129)	<0.05
LDL (<100 vs >100)	0.007(0.002 to 0.021)	<0.05

Analyzed by Chi-square test/ Fisher's exact test, *p value <0.05 was considered significant.

5. Discussion

There are increasing evidence from clinical studies suggesting associations between lower urinary tract symptoms(LUTS) and major chronic illnesses such as heart diseases, diabetes, and Metabolic Syndrome (MetS)[31]The presence of metabolic syndrome was associated with higher IPSS total scores (21.86) compared to the subjects with no MetS (15.91). Our study found that improvement in IPSS score was better in the MetS –ve subjects (0.78) compared to the other group (1.44) [Table-6].This study showed that MetS had a negative impact on the overall response to medical treatment of BPH similar to the results obtained with Kupelian et al[32]& Lee YC et al[33] who showed that MetS had a significantly negative impact on the responsiveness to α1-blocker in men with BPH/LUTS. Prostate volume differed significantly between patients with and without MetS (54.20cc vs. 28.06 cc) [Table-6] which corroborates with another study by Koo et al[34] and Hammarsten et al.[35] Lower HDL cholesterol, increased triglycerides above 1.7 mmol/l and higher LAP Score (67.29 vs. 35.74) [Table-3&4] was seen among those with MetS than in those without MetS. Significantly higher insulin levels and HOMA-IR(5.49 vs. cut-off of 2.77) in MetS +ve as compared to MetS-ve subjects(2.34) as supported by Kasturi et al, 2006 [Table-4]. HOMA-IR is an insulin like growth factor, a known prostatic mitogen. Several recent studies have provided convincing evidence of a possible role of MetS, and/or its individual components, in the development of BPH, prostate growth, and worsening of LUTS.[36]

6. Conclusion

Our study confirmed the frequent coexistence of MetS and BPH. This association seems to be a consequence of the MetS-related changes in the clinical symptoms and metabolic derangements. MetS negatively affects the response to medical treatment of BPH. Therefore, it is necessary to consider MetS as a potential risk factor in treating pts with BPH. Further long term studies with larger sample size are needed to substantiate the above findings. Our study emphasizes that MetS evaluation should be an integral part of the standard assessment of male patients with LUTS as well as a new domain in clinical and basic research. Treating physicians need to be cognizant of the impact that MetS has on urologic diseases as well as on overall patient health.

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8. Conflict of Interest

The authors declare they have no conflict of interest.

References

1. American Urological Association Guideline. Management of Benign Prostatic Hyperplasia (BPH). American Urological Association; 2010.

2. Shah AK, Srivastava A, Karan SC. Medical management of patients with benign prostatic hyperplasia: A study in Indian population. *J Mar Med Soc*. 2018;20(2):104–10. doi:10.4103/jmms.jmms_22_18.
3. Yu S, Guo X, Yang H, Zheng L, Sun Y. An update on the prevalence of metabolic syndrome and its associated factors in rural Northeast China. *BMC Public Health*. 2014;14:877.
4. Selvaraj I, Gopalakrishnan S, Logaraj M. Prevalence of metabolic syndrome among rural women in a primary health centre area in Tamil Nadu. *Indian J Public Health*. 2012;56(4):314–7. doi:10.4103/0019-557x.106423.
5. Pathania D, Bunger R, Bunger E, Mishra P, Arora A. An epidemiological study of metabolic syndrome in a rural area of Ambala district, Haryana. *J Family Community Med*. 2014;21(2):130–3. doi:10.4103/2230-8229.134774.
6. Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults. Executive summary of the Third Report of the National Cholesterol Education Program (NCEP) Expert Panel on Detection, Evaluation, and Treatment of High Blood Cholesterol in Adults (Adult Treatment Panel III). *Expert Panel Detection*. 2001;285(19):2486.
7. Robert G, Descazeaud A, de la Taille A. Lower urinary tract symptoms suggestive of benign prostatic hyperplasia: who are the high-risk patients and what are the best treatment options? *Curr Opin Urol*. 2011;21(1):42–8. doi:10.1097/mou.0b013e32834100b3.
8. Nunzio CD, Aronson W, Freedland SJ, Giovannucci E, Parsons JK. The Correlation Between Metabolic Syndrome and Prostatic Diseases. *Eur Urol*. 2012;61(3):560–70. doi:10.1016/j.eururo.2011.11.013.
9. Yat-Ching T. Male Lower Urinary Tract Symptoms/Benign Prostatic Hyperplasia and Metabolic Syndrome:Review. *Incont Pelvic Floor Dysfunct* . 2009;3(2):49–51.
10. Abdollah F, Briganti A, Suardi N. Metabolic Syndrome and Benign Prostatic Hyperplasia: Evidence of a Potential Relationship, Hypothesized Etiology, and Prevention. *Korean J Urol*. 2011;52:507–16.
11. Zhang X, Zeng X, Liu Y. Impact of Metabolic Syndrome on Benign Prostatic Hyperplasia in Elderly Chinese Men. *Urol Int*. 2014;93:214–9. doi:10.1159/000357760.
12. Michel MC, Mehlburger L, Schumacher H. EFFECT OF DIABETES ON LOWER URINARY TRACT SYMPTOMS IN PATIENTS WITH BENIGN PROSTATIC HYPERPLASIA. *J Urol*. 2000;163:1725–29. doi:10.1016/s0022-5347(05)67529-5.
13. Lee YC, Liu CC, Juan YS, Wu. The impact of metabolic syndrome on the responsiveness to α1-blocker in men with BPH/LUTS. *Int J Clin Pract*. 2013;67(4):356–62.
14. Nandy PR, Saha S. Association between components of metabolic syndrome and prostatic enlargement: An Indian perspective. *Med J Armed Forces India*. 2016;72(4):350–5. doi:10.1016/j.mjafi.2016.07.005.
15. Duskova M, Hill M, Starka L. Changes of metabolic profile in men treated for androgenetic alopecia with 1 mg finasteride. *Endocr Regulations*. 2010;44(1):3–8. doi:10.4149/endo_2010_01_3.
16. Duskova M, Hill M, Starka L. Changes of metabolic profile in men treated for androgenetic alopecia with 1 mg finasteride. *Endocr Regul*. 2010;44(1):3–8. doi:10.4149/endo_2010_01_3.
17. Wang CC, Liao CH, Liu HT, Lin JM, Kuo HC. Association of urinary nerve growth factor levels with erectile function in young men with type 2 diabetes mellitus. *Ci Ji Yi Xue Za Zhi*. 2017;29(1):1–5. doi:10.4103/tcmj.tcmj_2_17..
18. Gravas S, Dimitropoulos K. New therapeutic strategies for the treatment of male lower urinary tract symptoms. *Res Rep Urol*. 2016;8:51–9. doi:10.2147/rru.s63446.
19. Roehrborn CG, Siami P, Barkin J, Damião R, Major-Walker K, Nandy I, et al. The Effects of Combination Therapy with Dutasteride and Tamsulosin on Clinical Outcomes in Men with Symptomatic Benign Prostatic Hyperplasia: 4-Year Results from the CombAT Study. *Eur Urol*. 2010;57(1):123–31. doi:10.1016/j.eururo.2009.09.035.
20. Lepor H, Kazzazi A, Djavan B. α-Blockers for benign prostatic hyperplasia. *Curr Opin Urol*. 2012;22(1):7–15. doi:10.1097/mou.0b013e32834d9bfd.
21. Lawrentschuk N, Perera M. Benign prostate disorders. Dartmouth (MA: MDText.com, Inc; 2000-2018.
22. European Association of Urology Guidelines. Treatment of non-neurogenic male LUTS; 2018.
23. American Urological Association. American Urological Association guideline: management of benign prostatic hyperplasia (BPH). Linthicum (MD): American Urological Association Education and Research, Inc.; . 2010;.
24. Huang PL. A comprehensive definition for metabolic syndrome. *Dis Model Mech*. 2009;2(5-6):231–7. doi:10.1242/dmm.001180.
25. Sumner AE, Cowie CC. Ethnic differences in the ability of triglyceride levels to identify insulin resistance. *Atheroscler*. 2008;196(2):696–703. doi:10.1016/j.atherosclerosis.2006.12.018.
26. Gravas S, Bachmann A, Descazeaud A, Drake M, Gratzke C, Madersbacher S, et al. Guidelines on the management of non-neurogenic male lower urinary tract symptoms (LUTS), incl. benign prostatic obstruction (BPO). *Eur Assoc Urol*. 2014;.
27. Miccoli R, Bianchi C, Odoguardi L, Penno G, Caricato F, Giovannitti MG, et al. Prevalence of the metabolic syndrome among Italian adults according to ATP III definition. *Nutr Metab Cardiovasc Dis*. 2005;15(4):250–4. doi:10.1016/j.numecd.2004.09.002.
28. Ioachimescu AG, Brennan DM, Hoar BM, Hoogwerf BJ. The Lipid Accumulation Product and All-cause Mortality in Patients at High Cardiovascular Risk: A PreCIS Database Study. *Obesity*. 2010;18(9):1836–44. doi:10.1038/oby.2009.453.
29. Maturana MA, Moreira RMC, Spritzer PM. Lipid accumulation product (LAP) is related to androgenicity and cardiovascular risk factors in postmenopausal women. *Maturitas*. 2011;70(4):395–9. doi:10.1016/j.maturitas.2011.09.012.
30. Raza I, Hassan N, Jafri A, Gul P. Relationship between Benign Prostatic Hyperplasia and International Prostatic Symptom Score. *Br J Med Med Res*. 2015;10(5):1–9. doi:10.9734/bjmmr/2015/19965.
31. National Institute of Health and Clinical Excellence (NICE). The management of lower urinary tract symptoms in men. London: National Health Services. 2010;.
32. Kupelian V, McVary KT, Kaplan SA, Hall SA, Link CL, Aiyer LP, et al. Association of Lower Urinary Tract Symptoms and the Metabolic Syndrome: Results From the Boston Area Community Health Survey. *J Urol*. 2013;189(1S). doi:10.1016/j.juro.2012.11.026.
33. Lee YC, Liu CC, Juan YS. The impact of metabolic syndrome on the responsiveness to α1-blocker in men with BPH/LUTS. *Int J Clin Pract*. 2013;67(4):356–62.
34. Koo KC, Cho KS, Kang EM, Kwon SW, Hong SJ. The relationship between metabolic syndrome and prostate volume in men over sixties who underwent prostate health check-up. *Korean J Urol*. 2008;49:813–7.
35. Hammarsten J, Högstedt B, Holthuis N, Mellström D. Components of the metabolic syndrome—risk factors for the development of benign prostatic hyperplasia. *Prostate Cancer Prostatic Dis*. 1998;1(3):157–62. doi:10.1038/sj.pcan.4500221.
36. Nunzio CD, Aronson W, Freedland SJ, Giovannucci E, Parsons JK. The Correlation Between Metabolic Syndrome and Prostatic Diseases. *Eur Urol*. 2012;61(3):560–70. doi:10.1016/j.eururo.2011.11.013.

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