OBSERVATIONS

Acute Myocardial Infarction Masked by Brugada Syndrome: A Case Report

Background: Brugada syndrome is characterized by abnormal findings on electrocardiography and an increased risk for sudden cardiac death (1). The distinctive electrocardiographic finding is a coved ST-segment elevation in V_1 to V_3 that is more than 2 mm high followed by a negative T wave, although other findings have been reported. Ventricular tachycardia and fibrillation are the mechanisms for sudden cardiac death, which occurs more frequently in men (especially those in their early 40s) and perhaps in persons from Asia. Brugada syndrome is believed to be a genetic disorder because it also occurs more frequently in some families and because some patients have genetic mutations that affect the cardiac sodium channel or other ion channels. However, the yield of genetic testing is limited. This condition was first described in 1992 and is being recognized more frequently for uncertain reasons.

Purpose: To alert clinicians to the difficulty of diagnosing acute myocardial infarction in some patients with Brugada syndrome.

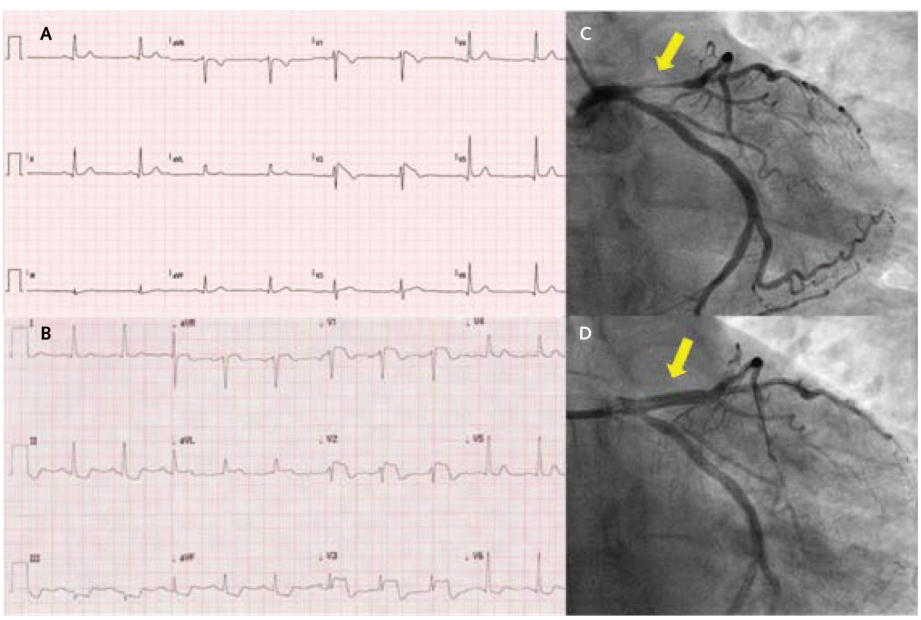
Case Report: We provided care for a 60-year-old white woman with Brugada syndrome. Her electrocardiogram showed changes in the anterior leads consistent with type 1 Brugada syndrome (**Figure**, *panel A*) (2). The patient has never had syncope and has no family history of sudden death.

Two years ago, she developed new-onset central chest pain. Positive results on an exercise test prompted coronary angiography, which showed a severe lesion in the proximal left anterior descending artery. This lesion was treated with angioplasty and a drug-eluting stent. She recovered completely, and her electrocardiogram was unchanged after the episode.

The patient was admitted recently with new chest pain and new electrocardiographic findings (**Figure**, *panel B*). We suspected an acute anterior infarction, but interpretation of her electrocardiogram was complicated by persistent changes on it from Brugada syndrome. Urgent angiography revealed a subocclusive thrombosis of the stent with unobstructed left main stem, circumflex, and right coronary arteries (**Figure**, *panel C*). Another angioplasty was done (**Figure**, *panel D*), and she has since returned to her usual clinical status.

Discussion: Diagnosing an acute myocardial infarction with ST-segment elevation is complicated in some patients with other medical conditions that affect the electrocardiogram, such as cardiomyopathy, pericarditis, electrolyte disturbances, and early repolarization pattern, and in some African-Caribbean patients (3). We believe that this case report adds Brugada syndrome to the list. A detailed medical history and comparison of the patient's current electrocardiogram with previous ones is crucial to make the correct diagnosis and avoid delays in urgent cardiac catheterization. If the patient has Brugada syndrome, looking for new horizontal ST elevations and mirror ST depressions is especially important.

Figure. Findings on electrocardiography and angiography in a patient with Brugada syndrome and anterior myocardial infarction.



A. Coved ST-segment elevation in V_1 and V_2 that is >2 mm high. **B.** Changes during the recent episode of chest pain include a different morphologic characteristic of the ST-segment elevation in V_1 and V_2, extension of ST-segment elevation into V_3 and aVL, and mirror ST depressions in inferior leads II, III, and aVF. **C.** Angiogram focusing on the proximal left anterior descending artery (*arrow*) before angioplasty. **D.** Angiogram focusing on the proximal left anterior descending artery (*arrow*) after angioplasty.

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Sodium–Glucose Cotransporter 2 Inhibitor Improves Complications of Lipodystrophy: A Case Report

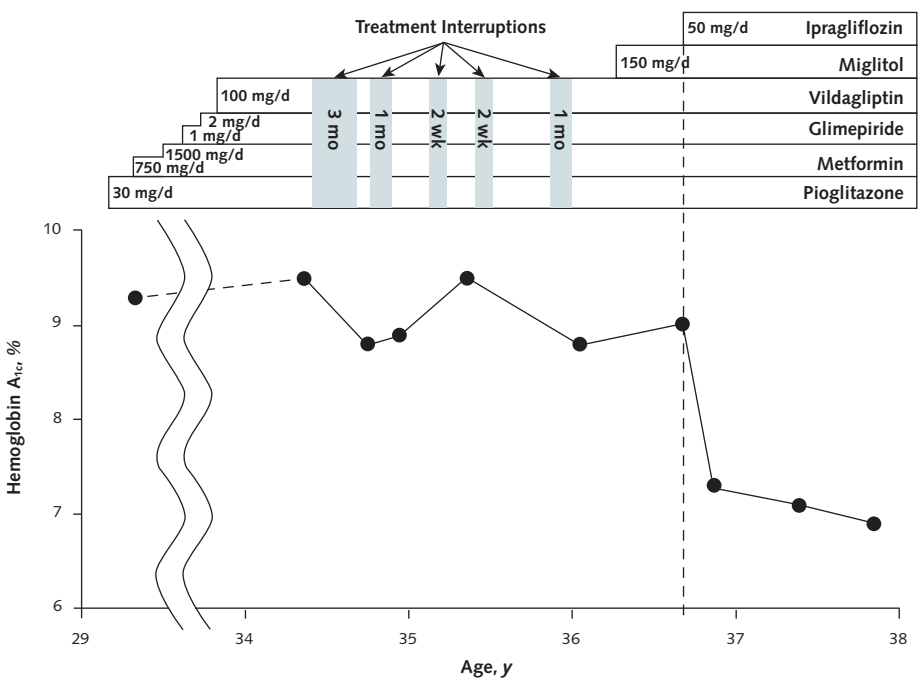
Background: Lipodystrophies are characterized by selective loss of adipose tissue, which leads to fatty liver, insulin resistance, and other complications (1). Lipodystrophies can be acquired or inherited. Infection with HIV may be the best known cause of acquired lipodystrophy, but congenital generalized lipodystrophy is the most severe form. Antidiabetic agents, such as metformin, sulfonylureas, and insulin, often fail to improve glycemic control in patients with lipodystrophy because of the severity of insulin resistance. Leptin improves the complications associated with lipodystrophy (2, 3) but is expensive and requires subcutaneous injections, which are painful because of the lack of subcutaneous adipose tissue (4). Therefore, inexpensive alternative therapies that do not require injection are eagerly awaited.

Objective: To describe effective treatment of the complications associated with lipodystrophy using ipragliflozin, a sodium–glucose cotransporter 2 inhibitor.

Case Report: We cared for a patient with near-complete lack of body fat from birth. At age 15 years, he was diagnosed with diabetes at our hospital and started glimepiride therapy. At that time, he was also diagnosed with type 2 congenital generalized lipodystrophy due to a homozygous nonsense mutation at codon 275 of the *BSCL2* gene. Soon afterward, he stopped coming to our hospital.

The patient returned at age 29 years and at that time was not taking any medications for his diabetes. His fasting plasma glucose level was 11.9 mmol/L (214 mg/dL) with a hemoglobin A_{1c} (HbA_{1c}) level of 9.3%. His body mass index was 20.4 kg/m^2. He had severe insulin resistance with a fasting insulin

Figure. Hemoglobin A_{1c} levels before and after starting ipragliflozin therapy.



level of 192 pmol/L and a homeostasis model assessment of insulin resistance score of 14.6. Computed tomography (CT) showed severe hepatic steatosis. His HbA_{1c} level remained around 9% despite treatment with several antidiabetic medications, which he repeatedly interrupted (**Figure**). He began receiving insulin therapy but immediately stopped because of injection pain. He declined leptin because of its high cost.

At age 36 years, he started ipragliflozin therapy. His HbA_{1c} level immediately decreased markedly (**Figure**). In addition, CT performed 6 months later revealed a normal liver–spleen ratio, which suggested regression of hepatic steatosis. Plasma and urinary ketone levels did not increase. The cross-sectional areas of his psoas muscles, as measured on CT, did not decrease, and he reported no symptoms related to muscle weakness at any time during treatment with ipragliflozin. Fourteen months after he started this agent, his HbA_{1c} level was 6.9%, fasting plasma glucose level was 7.4 mmol/L (133 mg/dL), and insulin level was 48 pmol/L, and he had a homeostasis model assessment of insulin resistance score of 2.27.

Discussion: Adding ipragliflozin therapy to other medications dramatically decreased this patient's insulin resistance as measured by the homeostasis model assessment of insulin resistance and led to regression of fatty liver as measured by normalization of the liver–spleen ratio on CT. He received this agent for more than 1 year with no apparent adverse effects. Ipragliflozin and other sodium–glucose cotransporter 2 inhibitors enhance urinary glucose excretion, which shifts substrate utilization from carbohydrate to fat (5), and this mechanism may explain this patient's improvement in both insulin resistance and diabetes. Therefore, we propose that sodium–glucose cotransporter 2 inhibitors are a rational therapeutic option for lipodystrophy-associated metabolic disorders on the basis of their mechanism of action, economic benefits, and ability to improve adherence.

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Trends in Prostate-Specific Antigen Screening and Prostate Cancer Interventions 3 Years After the U.S. Preventive Services Task Force Recommendation

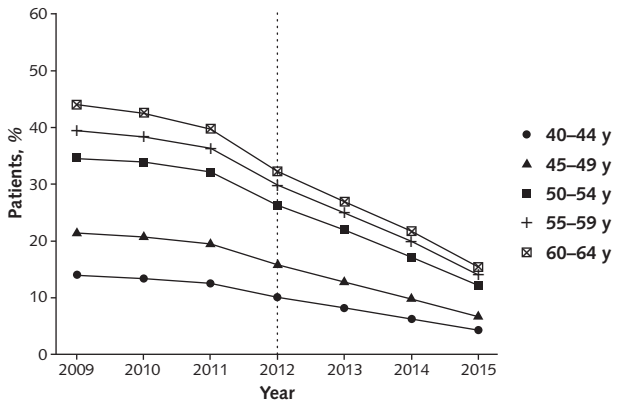
Background: In 2012, the U.S. Preventive Services Task Force (USPSTF) advised against routine prostate-specific antigen (PSA) screening for prostate cancer in asymptomatic men (1). Studies reported a substantial decline in the prevalence of PSA screening 1 year after the recommendation was published (2–5). We sought to measure whether this change persisted and whether trends in prostate cancer treatment have changed.

Methods: We examined routine use of PSA screening and prostate cancer treatment before and after publication of the 2012 USPSTF recommendation (between 2009 and 2015) using claims from Aetna, a commercial health insurer in the United States. The Boston Children's Hospital institutional review board approved the study and granted a waiver of consent. Participants were men aged 40 to 64 years enrolled in the health care plan for at least 1 year. To form a cohort of asymptomatic men who had routine PSA screening as opposed to diagnostic PSA testing, we excluded those with a history of prostate cancer, prostatectomy, androgen deprivation therapy, and elevated PSA levels. We also excluded men who presented with symptoms in the 6 months before PSA testing, including urinary obstruction, prostatitis, hematuria, other prostate disorders, unexplained weight loss, and back pain. Diagnoses and procedures were identified using International Classification of Diseases, Ninth Revision; CPT (Current Procedural Terminology); and Healthcare Common Procedure Coding System codes. Analyses were stratified by age group in years (40 to 44, 45 to 49, 50 to 54, 55 to 59, and 60 to 64) and region (Northeast, South, Midwest, and West). Statistical analyses were performed using SPSS, version 23 (IBM).

Results: A total of 16 007 754 men qualified for our cohort. After the 2012 USPSTF recommendation against PSA screening was published, a sustained downward trend in screening was observed across all age groups (**Figure**) and regions (**Appendix Table** and **Appendix Figure 1**, available at Annals.org). Among those screened, a sustained downward trend in diagnostic biopsy, prostatectomy, and radiation therapy after the PSA test was noted; no clear trend was observed in androgen deprivation therapy (**Appendix Figure 2**, available at Annals.org).

A comparison of the years 2011 and 2015 shows that the decline in PSA screening rate was greatest among men aged 60 to 64 years (absolute difference, 24.1% [95% CI, 24.0% to 24.3%]) and lowest among those aged 40 to 44 years (absolute difference, 8.3% [CI, 8.2% to 8.4%]). Of the 4 regions, PSA screening decreased most in the South (absolute difference, 17.4% [CI, 17.3% to 17.5%]) and least in the Midwest (absolute difference, 14.6% [CI, 14.5% to 14.7%]). The rate of follow-up diagnostic biopsy decreased from 1.4% to 0.9% (absolute difference, 0.5% [CI, 0.5% to 0.6%]). The proportion of men undergoing prostatectomy and radiation therapy declined from 0.3% to 0.2% and 0.4% to 0.2%, respectively. Prostate cancer interventions decreased most in the last year, between 2014 and 2015.

Figure. Trends in PSA screening among asymptomatic men aged 40–64 y enrolled with a major national health insurer.



PSA = prostate-specific antigen.

Discussion: Three years after the 2012 USPSTF recommendation was published, the PSA screening rate among men aged 40 to 64 years declined substantially. Among those who were screened, prostate cancer interventions also declined substantially. These trends suggest that the recommendation influenced not only screening practices but also treatment strategies. An increased awareness of the limitations of PSA screening may have steered clinicians toward more conservative biopsy referral criteria and the referral of low-risk cases to active surveillance instead of more invasive management approaches involving surgery and radiation therapy. Future studies will need to examine whether practice changes are associated with mortality trends.

The PSA screening rate in fact began to decline before the 2012 USPSTF recommendation was published (**Figure**). This may reflect increased awareness of the limitations of screening after the publication of 2 large randomized, controlled trials in 2009 (the PLCO [Prostate, Lung, Colon and Ovarian] cancer screening trial in the United States and the ERSPC [European Randomized Study of Prostate Cancer]) showing that PSA screening had limited to no mortality benefits. These trials were followed by an updated guideline by the American Cancer Society in 2010, highlighting the potential harms of PSA screening and emphasizing the need for shared and informed decision making, and the release of a draft guideline by the USPSTF in late 2011. These events may have culminated in the observed downward trends in PSA screening before 2012.

Our study cannot establish causality and is limited to a single insurer. Our data set also does not capture racial differences in PSA screening. However, our study population is geographically diverse and the data presented here are probably broadly generalizable to the commercially insured population in the United States. Moreover, because all procedures are systematically captured, our study is not subject to the coverage and recall biases that may have affected previous studies (2–5) based on the National Health Interview Survey.

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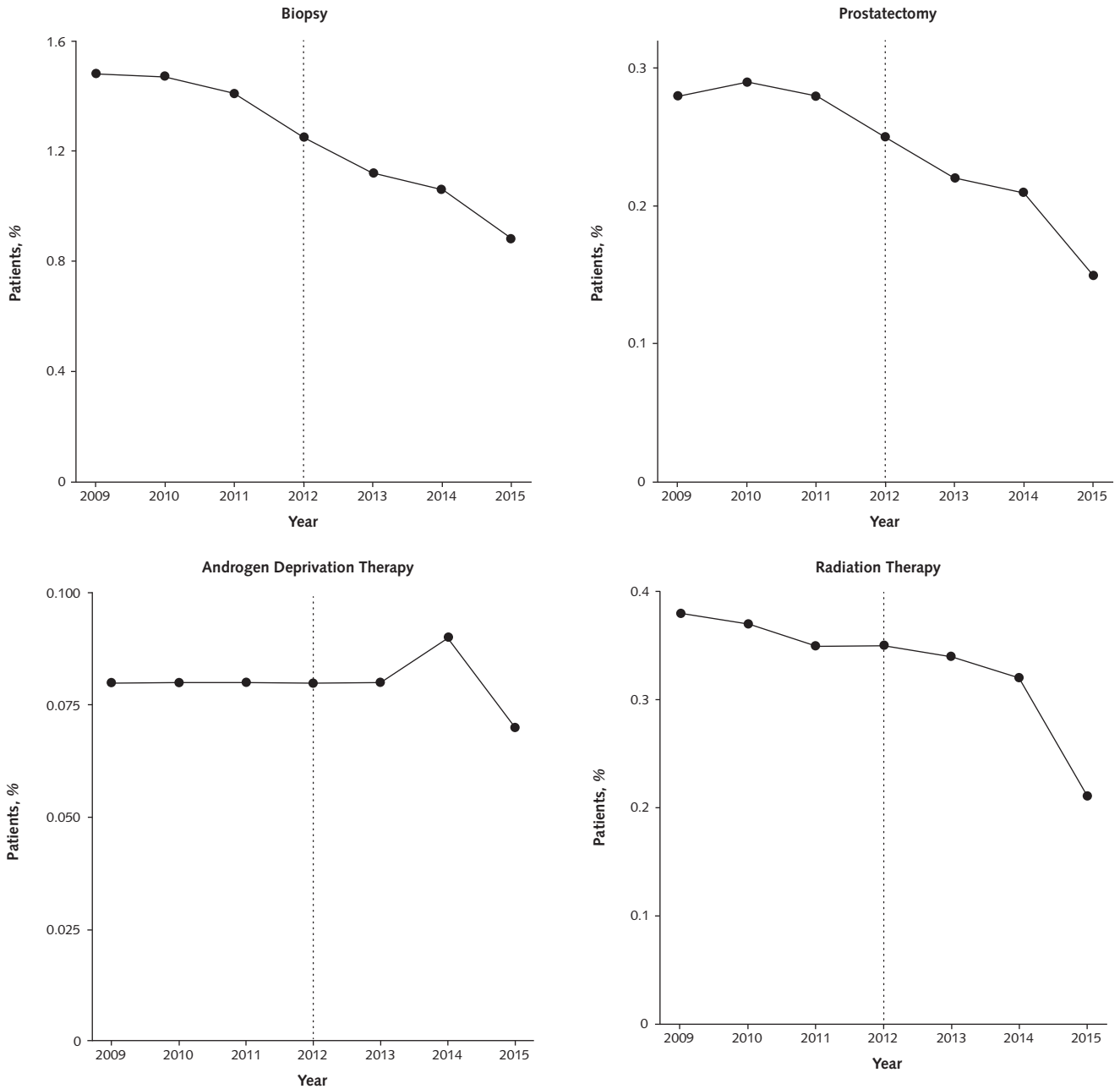
Appendix Table. Study Population of Men Aged 40–64 y Enrolled in a Major National Health Insurer

Variable	Age Group, *n* (%)					Region, *n* (%)*			
	40–44 y	45–49 y	50–54 y	55–59 y	60–64 y	Northeast	South	Midwest	West
2009	558 524 (21.3)	603 659 (23.0)	570 586 (21.8)	485 082 (18.5)	402 377 (15.4)	676 132 (25.8)	10 94 569 (41.8)	403 573 (15.4)	442 815 (16.9)
2010	619 841 (21.2)	659 656 (22.5)	642 365 (21.9)	551 766 (18.8)	454 177 (15.5)	744 644 (25.4)	12 14 080 (41.4)	463 895 (15.8)	512 363 (17.5)
2011	611 833 (21.1)	633 729 (21.9)	636 189 (22.0)	557 035 (19.2)	456 110 (15.8)	743 687 (25.6)	11 88 566 (41.0)	461 547 (15.9)	508 613 (17.5)
2012	662 657 (20.9)	677 245 (21.4)	697 434 (22.0)	625 174 (19.8)	502 418 (15.9)	815 776 (25.7)	12 80 712 (40.4)	508 733 (16.0)	565 246 (17.8)
2013	751 746 (20.6)	765 395 (21.0)	802 737 (22.0)	734 862 (20.2)	591 055 (16.2)	942 403 (25.8)	14 69 944 (40.3)	574 654 (15.8)	658 708 (18.1)
2014	903 481 (20.4)	921 718 (20.8)	969 343 (21.9)	899 380 (20.3)	734 590 (16.6)	11 21 406 (25.3)	18 04 461 (40.7)	676 878 (15.3)	831 329 (18.7)
2015	117 7670 (19.7)	12 41 872 (20.8)	12 87 908 (21.6)	12 29 905 (20.6)	10 31 436 (17.3)	14 13 075 (23.7)	24 76 317 (41.5)	10 21 218 (17.1)	10 51 294 (17.6)
Absolute reduction in PSA screening rates (2011 vs. 2015) (95% CI), %	8.3 (8.2–8.4)	12.7 (12.6–12.8)	20.1 (19.9–20.2)	22.1 (22.0–22.3)	24.1 (24.0–24.3)	17.0 (16.9–17.1)	17.4 (17.3–17.5)	14.6 (14.5–14.7)	15.9 (15.8–16.1)

PSA = prostate-specific antigen.
* Data may not sum to the total patients because ZIP code data were unavailable for 0.02% of patients and 0.1% of patients had multiple ZIP codes.

Appendix Figure 1. Trends in prostate cancer screening, by region.

Appendix Figure 2. Prostate biopsy and interventions among patients who had PSA screening.



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