U Waves Inversion In Correlation With The Presence Of Stenosis Of The Left Anterior Descending / Left Main Coronary Artery: A Systematic Review

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Abstract

Background: U wave inversion and presence of stenosis of left anterior descending/left main coronary remains unclear. When this wave can be considered for diagnosis, influencing factors, and the patient's clinical condition, there are still no papers that discuss it
Methods: A systematic search was conducted through PubMed/MEDLINE and ScienceDirect databases. This systematic review used all studies in the field of U wave inversion in correlation with the presence of stenosis of left anterior descending/left main coronary artery indefinitely.
Result: The search yielded 22 studies involving a total of 2637 patients were obtained for the present study. About 11 studies reported exercise induced U waves, while 8 studies reported U wave in resting patients. The presence of U wave was frequently found in patients during angina attack, however 6 studies reported U wave in absence of angina attack patients. The incidences of U wave inversion in LAD stenosis were reported in 14 studies, 2 studies reported the presence of prominent U wave in LAD stenosis, and 4 studies reported both waves were found in patients with LAD stenosis. About 13 studies reported angina attack in patients with LAD narrowing.
Conclusion: Inverted U waves are associated with the incidence of LAD/LMCA stenosis and are more common than prominent U waves in patients with symptomatic chest pain. These waves can be identified in patients either at rest or during exercise testing.

Keywords: U wave inversion, stenosis, left anterior descending, left main coronary artery

1. Introduction

U wave inversion on the 12 lead electrocardiogram is rarely seen in the absence of significant cardiac disease[1]. However, there are still differences of opinion regarding the diagnostic importance of this wave including for the initial diagnosis of left anterior descending/left main coronary artery stenosis. Several studies have shown that only resting U wave inversion can be used as a diagnostic tool. While several other studies explain the need for exercise induction to get a U wave inversion so that it can be used as a diagnostic guideline[2]. The patient's medical history and symptoms during cardiac recording also have the potential to correlate with the presence of U wave inversion as a predictor of left anterior descending/left main coronary artery stenosis. The aim of this paper is to review the diagnostic importance of U-wave inversion in left anterior descending/left main coronary artery stenosis.

2. Methods

2.1 Searching Strategy

This systematic review used all studies in the field of U wave inversion in correlation with the presence of stenosis of left anterior descending/left main coronary artery indefinitely. Existing studies were identified by two independent reviewers (CFA and AT) through PubMed and ScienceDirect databases using the search terms “U Wave Inversion AND Stenosis AND Left Anterior Descending OR Left Main Coronary Artery”. Also, manual searches for additional articles were performed. Abstract and full text was reviewed by four authors (CFA, AT, and ZE). The authors were contacted for supplementary information if there were incomplete data from the full texts. Disagreements were resolved through debate.

2.2 Selection Criteria

Inclusion criteria (the guidelines to select the eligible studies which could be included in the process of the analysis) and exclusion criteria were chosen as follows.

2.2.1 Inclusion Criteria

(1) Human subjects (2) Resting or exercise induced (3) ECG shows U wave inversion (4) Diagnosed with stenosis of the left anterior descending / left main coronary artery

2.2.2 Exclusion Criteria

(1) Non-English language published studies (2) Non related studies to inverted U waves in correlation with the presence of stenosis of the left anterior descending / left main coronary artery (3) Inadequate/Unavailable data and repeated studies

2.3 Data Extraction and Quality Assessment

After a careful review of the included studies, details were obtained from the articles which qualified for final inclusion. The following important headings were extracted from these studies: Journal author, publication year, country, population study, sample size, sample age, underlying disease, medication, resting or exercise induced, clinical features, presence of U wave inversion, diagnosed stenosis LAD/LMCA.

3. Results

3.1 Overview of Literature Searching

There were 1377 studies identified through database searching from Pubmed and Sciencedirect. We screened 1087 titles and abstracts after removing duplicates, leaving 22 studies to be selected and then analyzed for qualitative synthesis. Figure 1.

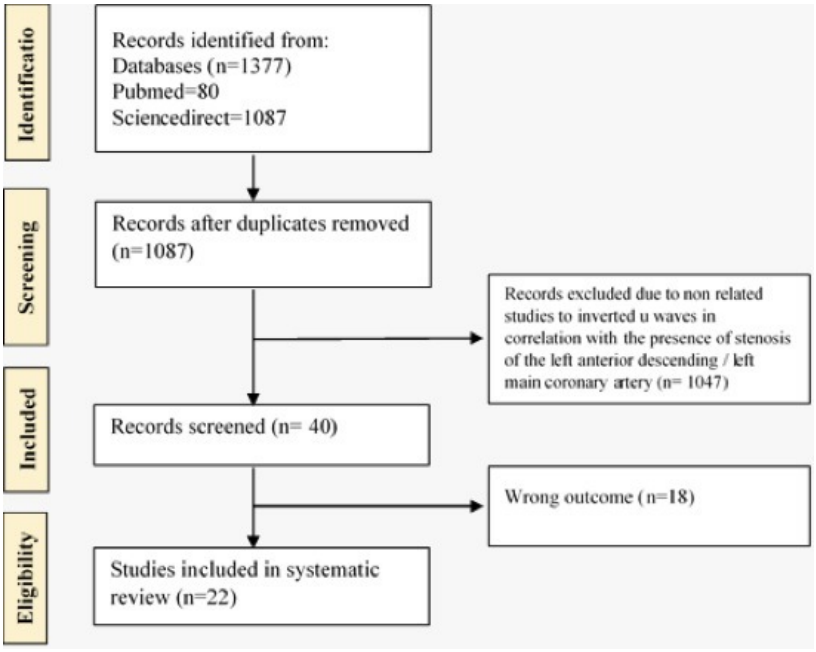

Figure 1. PRISMA flowchart of the literature selection

3.2 Study Characteristics

In this review, 22 studies were included. A total 2637 of participants were enrolled in the study of U waves inversion in correlation with the presence of stenosis of the left anterior descending/left main coronary artery. Table 1.

Table 1. Main Characteristics of Reviewed Studies

Author, year	Sample Size	Sample Age	Underlying Disease	Medication	When the ECG recorded	Clinical Features	Presence of U wave inversion	Diagnosis stenosis LAD / LMCA
Gurlek et al, 1994	112	52 ± 9.33	UAP (48)	Not mentioned	Right before cardiac catheterization	Chest pain	(26) + U waves, (22) - U waves	Multivessel disease with severe left anterior descending lesions in - U waves
		51.5 ± 5.63	Inferior MI (20)				(8) + U waves, (12) - U waves	-
		53 ± 7.85	Anterior MI (35)				(15) + U waves, (20) - U waves	Multivessel disease with severe left anterior descending lesions in - U waves
		52.25 ± 6.95	Non-Q wave MI (9)				(3) + U waves, (6) - U waves	-

Cia et al, 1987	1	50	UAP	Sublingual glyseril trinitrate, propanolol, isosorbide	During second episode of chest pain	Chest pain	U wave inversion in leads I, V4 and V5, isoelectric U waves in leads V3, V6 and AVL, flat U wave in lead V2 and upright U waves in leads III and AVF	99% stenosis of the left main coronary artery (LMCA)
Chikamori et al, 1994	311	63 ± 8	Suspected CAD with no previous myocardial infarction	Not mentioned	After treadmill exercise	Chest pain, ST-segment depression, or submaximal heart rate (85% of the age-predicted maximal heart rate-s) was regarded as an indication for stopping exercise	(91) Prominent + U waves	Right and left precordial leads, sensitivity 52%, specifity 88%, accuracy 72%, predictive value 77%
		61 ± 9					(220) No Prominent U waves	-
Chikamori et al, 1994	102	LAD (61±9) LC (64±7) RCA (63±7)	Suspected CAD with no previous myocardial infarction	Not mentioned	After treadmill exercise	Chest pain, ST-segment depression, or submaximal heart rate (85% of the age-predicted maximal heart rate-s) was regarded as an indication for stopping exercise	- U waves	LAD (16/66), LC (1/24), RCA (2/13)
							Prominent U waves	LAD (8/66), LC (11/24), RCA (8/13)
Chikamori et al, 1996	264	65 ± 8	Anterior wall AMI (207)	Nitrates, calcium antagonist	After treadmill exercise	Chest pain, ST-segment depression, or submaximal heart rate (85% of the age-predicted maximal heart rate-s) was regarded as an indication for stopping exercise	Prominent U waves	LAD (14/31), RCA (30/31), Inferior/Posterior reversible defects (24/31)

		66 ± 11	Inferior and posterior wall AMI (61)				No Prominent U waves	LAD (11/31), RCA (22/31), Inferior/Posterior reversible defects (10/31)
Chikamori et al, 1997	339	61	Severe left anterior descending artery narrowing of >90%	No digitalis and beta blocker	After treadmill exercise	Chest pain, ST-segment depression, or submaximal heart rate (85% of the age-predicted maximal heart rate-s) was regarded as an indication for stopping exercise	U wave inversion after exercise	LAD stenosis 90% (5), 99% (12), 100% (30)
Friedberg et al, 1968	1	36	History of retrosternal pressure on exercise and two episodes of prolonged chest pain		Exercise induced	Physical examination was normal	U wave inversion after exercise	Complete stenosis LAD
Galli et al, 1989	1	34	Not mentioned	Nitrate, heparin, nifedipine	Exercise and dypiridamol induced	Chest pain	U wave inversion	Stenosis of the proximal LAD involving its first diagonal branch and the occlusion of the second LAD diagonal branch
Gerson et al, 1980	849	Not mentioned	Not mentioned	Long-acting nitrates, propanolol, digitalis	Resting patients	Chest pain	U wave inversion (27)	Stenosis LAD (24)
Gregory et al, 2006	1	47	Dypsneu on exertion	No medication	Resting patients	Denied any chest discomfort	U wave inversion in V2, V3	99% stenosis LAD
Jain et al, 1990	37	56,8	Previous infarction	Calcium antagonist, beta blocker, nitrates	During coronary angioplasty	-	Transient U wave inversion Transient U wave positive	During dilation 7 of 23 LAD, 4 of 9 LC, 1 of 11 RCA During dilation 12 of 23, 3 of 9 LC, 3 of 11 RCA

Kodama et al, 2002	ST elevation group (27)	66 ± 34	Hypertension, hypercholes-terolemia, smoking, diabetes	Not mentioned	After intracorona-ry injection of achetylco-line	-	New negative U wave (21)	Total occlusive LAD (10), Subcostal LAD (17)
	ST depression group (22)	73 ± 32					New negative U wave (17)	Total occlusive LAD (2), Subcostal LAD (20)
Kodama et al, 2000	60	63 ± 9	Angina pectoris on effort which lesion in LAD with U wave inversion (16)	Long-acting nitrate, CCB, B blocker, Potassium channel activator	During treadmill exercise	Chest pain	Transient U wave inversion	Proximal LAD (10/16), distal LAD (6/16)
		64 ± 8	Angina pectoris on effort which lesion in LAD with absent of U wave inversion (44)	Long-acting nitrate, CCB, B blocker, Potassium channel activator		Chest pain	Absent of U wave inversion	Proximal LAD (26/44), distal LAD (18/44)
Matsuguchi et al, 1982	1	44	OMI and hypertension	Sublingual nitrogly-ceri n	During chest pain	Chest pain	Transient U wave inversion	50% midportion LAD occlusion
Miwa et al, 1993	59	55.5 ±4.9	Variant angina pectoris (21)	Not mentioned	During chest pain and after cold test	Chest pain	Terminal U wave inversion (21), Initial U wave inversion (9)	Not mentioned
		Not mention-ed	Hypertension without CAD (38)	Not mentioned	After cold test	Denied any chest discomfort	Initial U wave inversion (38)	Not mentioned
Miwa et al, 2000	125	59 ± 8	Stable effort angina with Exercise-Induc ed U-Wave Changes (46)	Not mentioned	During rest, during exercise, and for the first 6 min after exercise	Chest pain during exercise (13)	Negative U wave (31), prominent U wave (15)	LAD (29/46), RCA (10/46), LCX (8/46)
		61 ± 11	Stable effort angina without Exercise-Induc ed U-Wave Changes (79)	Not mentioned		Chest pain during exercise (32)	No Prominent U waves (79)	LAD (42/79), RCA (22/79), LCX (21/79)

Lee et al, 2021	1	76	Wellens syndrome	Coronary artery bypass grafting	Resting	Denied any chest discomfort	U wave inversion	Proximal LAD
Salmasi et al, 1985	160	49.3 ± 9.6	Occlusion or >50% stenosis in any coronary artery (133)	B blocker (89), no digoxin	During exercise and after exercise	Chest pain	U wave inversion (21/133)	LAD (126/133), LCX (99/133), RCA (91/133)
			Normal coronary arteries (27)	Not mentioned		Denied any chest discomfort	U waves (0/27)	-
Scholl et al, 1987	2	40	Class III effort angina	Not mentioned	During exercise	Angina and arrhythmias (premature ventricular beats)	Negative U wave	80% proximal LAD occlusion, 80% proximal circumflex artery occlusion
		36	Class III effort angina	Not mentioned		Angina and arrhythmias (premature ventricular beats)	Negative U wave	Almost complete proximal LAD occlusion
Sovari et al, 2006	1	55	Hypertension and CAD	Heparin, metoprolol, aspirin, and simvastatin	During chest pain	Chest pain, shortness of breath and nausea	Negative U wave	25% distal LMCA occlusion, >90% proximal and mid LAD occlusion, and 65% RCA occlusion
Yano et al, 1987	102	29-70	Angina pectoris with coronary spasm (52)	Nitrate and CCB (withdrawn 24 h before provocation testing)	During exercise	Angina	Inverted U wave (46/52)	RCA (17/52), LAD (8/52), LCx (3/52), RCA+LAD (5/52), RCA+LCx (4/52), LAD+LCx (5/52), RCA+LAD+LCx (10/52)
		25-72	Angina pectoris with no coronary spasm (50)	Nitrate and CCB (withdrawn 24 h before provocation testing)		Angina	Inverted U wave (2/50)	RCA, LAD, LCx

		54,5	CAD with LAD lesion (41)	PTCA		Not mentioned	U wave inversion at resting (9/41), during PTCA procedure (31/41), total (37/41)	LAD (41/41)
Yano et al, 1991	59				During PTCA procedure			
		57,6	CAD with RCA lesion (18)	PTCA		Not mentioned	U wave inversion at resting (3/18), during PTCA procedure (12/18), total (16/18)	RCA (18/18)

4. Discussion

Although the mechanism of the U wave remains uncertain, U-waves inversion on the ECG are reported to be a specific marker of myocardial disease[1,3]. U-waves inversion are associated with hypertension, left ventricular hypertrophy, aortic and mitral regurgitation, cardiomyopathy, and may indicate myocardial ischemia[4]. U-waves inversion are commonly observed in patients with coronary artery disease (CAD)[5]. Several studies by Kodama et al, Chikamori et al, Gali et al, Miwa et al, Friedberg et al, and Scholl et al have reported exercise-induced U-wave inversion in myocardial infarction (MI) patients[2,6-13]. Others have reported the presence of transient U-wave inversion in resting patients with or without angina episodes[1,4,5,14-17]. According to Gurlek et al, U-wave inversion is a significant marker of stenosis. It may be present at rest or may be seen only during exercise testing. Both conditions may generate this wave[4].

According to the U-wave analysis, CAD patients could show prominent or inverted U-wave on ECG[10]. The previous studies reported U-wave inversion as the significance marker for artery stenosis[4]. In Gerson et al study, U-wave inversion was reported to be found in MI patients with left anterior descending coronary artery (LAD) narrowing[1]. Jain et al also reported negative U-wave on anterior MI patients with stenosis of the left main or proximal LAD[3]. Despite its low sensitivity for detecting LAD disease, the recent study by Kodama et al reported transient U-wave inversion in the precordial leads during exercise testing has been described as an electrocardiographic manifestation of myocardial ischemia in the territory of LAD[18]. Although U-wave inversion was also reported to be found on patients with multivessel stenosis[4]. Otherwise, prominent U-wave on patients with myocardial ischemia was infrequently mentioned. Based on study of exercise-induced U-waves, negative or prominent U-waves were reported to be beneficial in localizing coronary artery narrowing[9,10]. Chikamori et al discovered a prominent U-wave on the ECG of a MI patient following exercise, his recent study reported that prominent U-waves in the precordial leads during stress tests or spontaneous angina were considered as a marker for the left circumflex or right coronary artery narrowing[2,11].

Among the electrocardiographic signs of transient myocardial ischemia, U waves inversion in precordial leads have been reported to be very specific for coronary artery disease and to be almost

the hallmark of left anterior descending (LAD) coronary stenosis or spasm[5,11,17,19]. In the study that the authors analyzed qualitatively, apart from stenosis in LAD, stenosis or spasm was also found in other coronary arteries, namely the left circumflex artery (LCA) and right coronary artery (RCA)[4,5,13]. However, the highest number of inverted U waves found with chest pain was stenosis of the LAD as in the studies of Gurlek et al, Chikamori et al, Miwa et al, Lee Y et al, and Yano et al[2,4,9-11,13,20,21]. Meanwhile, in another study, it was found that when u wave inversion was found, only stenosis was found in the LAD and normal for other coronary arteries. These results are in a study conducted by Cia et al, Chikamori et al, Friedberg et al, Galli et al, Jain et al, Kodama et al, Matsuguchi et al, Scholl et al, and Yano et al. Many of the studies describe stenosis that occurs is more than 80% to total occlusion of the LAD. This can be explained that U-wave inversion in patients with chest pain can be an indication of multivessel disease with severe left anterior descending stenosis/spasm[3,6-8,14-16,18].

Of the 22 available studies, the most clinical presentation presented by patients at the appearance of U-wave inversions was chest pain[1,2,4,5,7-16,19,22]. The presence of inverted U waves accompanied by chest pain can be a sign of myocardial ischemia[14]. May be the earliest marker of unstable angina and evolving myocardial infarction[22]. Have been shown to predict a ≥ 75% stenosis of the LAD / LMCA and the presence of left ventricular dysfunction[15]. Meanwhile, several studies stated that there was no clinical presentation in the form of chest pain[3,6,17,18,20,21]. Friedberg et al in 1968 in their case report study stated that patients showed U-wave inversion after exercise induction and complete stenosis of the LAD, but with a normal physical examination without chest pain[6]. The same thing was also found in the studies of Gregory et al, Miwa et al, Lee Y et al, and Salmasi et al[13,17,19,21]. The mechanism of genesis of U wave is uncertain. The genesis may be different depending on the underlying disease[12,18]. In the study which stated that there was no chest pain during examination, all the patients involved had a history of diseases that have the potential to cause abnormalities in the work of the heart such as a history of retrosternal pressure on exercise and two episodes of prolonged chest pain, hypertension and wellens syndrome[21]. There is only one study conducted by Salmasi et al, involving patients without a history of coronary disease[19].

5. Conclusion

The study shows inverted U waves are associated with the incidence of LAD/LMCA stenosis and are more common than prominent U waves in patients with symptomatic chest pain. These waves can be identified in patients either at rest or during exercise testing. With this approach, stenoses are expected to be detected earlier and assist clinicians in making decisions for more appropriate investigations and management.

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