

# The Italian Implantable Cardioverter-Defibrillator Registry. A survey of the national activity during the years 2001-2003

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## Key words:

Implantable cardioverter-defibrillator; Registries; Sudden cardiac death.

**Background.** In recent years several trials demonstrated the efficacy of implantable cardioverter-defibrillator (ICD) therapy for sudden cardiac death prevention and total mortality reduction in particular high-risk groups of patients. The aim of this review was to report the main epidemiological data and the most important clinical characteristics of patients enrolled in the Italian ICD Registry in the years 2001-2003.

**Methods.** The Italian ICD Registry – official member of the Italian Association of Arrhythmology and Cardiac Pacing (AIAC) – collects 85% of the data concerning the national ICD implantation activity, based on the European Implantable Defibrillator form (EURID). Data are validated for quality of information and uniqueness at the moment of data entry and in successive steps at the time of the annual analysis.

**Results.** The number of ICDs implanted in Italy has been continuing to increase during the last years according to the general trend in European and non-European countries: 2400 in the year 2001, 3934 in the year 2002, and 5318 in the year 2003. The number of ICDs per million of inhabitants in Italy was 42.1 in the year 2001 (+11.8% with respect to 2000), 69.0 in the year 2002 (+63.9% with respect to 2001), and 93.3 in the year 2003 (+35.2% with respect to 2002). The number of implanting centers increased progressively from 273 in the year 2001 to 304 in the year 2002, and 340 in the year 2003. The median age of patients treated with ICD implantation was 67 years in the years 2001-2002, 68 years in the year 2003. The prevalence of male patients was significantly higher (79.3% in 2001, 82.3% in 2002, and 81.4% in 2003). The main indication was syncope (25.5, 29.3, and 32.9% in the years 2001, 2002, and 2003, respectively), followed by palpitations (17.7, 18.5, and 16.4% in the years 2001, 2002, and 2003, respectively), and cardiac arrest (10.0, 13.1, and 16.5% in the years 2001, 2002, and 2003, respectively). The use of ICD in patients considered at risk but without history of sustained ventricular tachycardia had a 3-fold increase during the 3 years, from 6.4% in 2001 to 18.2% in 2003. Ventricular tachycardia was the main arrhythmia in 50.4 to 55.0% of cases, ventricular fibrillation in 13.5 to 18.1%, both in 4.1 to 6.5%. The vast majority of patients presented at the enrolment either a mild or severe reduction in ejection fraction (30 to 50%, < 30%). Amiodarone was administered alone or in combination with antiarrhythmics in 29.7 to 40.0% of patients. Single-chamber ICDs were implanted in the years 2002 and 2003 in 45.7 and 39.2% of patients, dual-chamber ICDs in 34.9 and 32.4%, biventricular ICDs in 19.4 and 28.4%, respectively.

**Conclusions.** The ICD implantation rate in Italy increased significantly in the period 2001-2003, similarly to the trend in the other western countries and following the publication of controlled studies in the field of primary and secondary prevention of sudden cardiac death. The Italian ICD Registry showed during the last 3 years an important increase in prophylactic ICD utilization. A sophisticated ICD, including dual-chamber pacing or cardiac resynchronization therapy, was chosen in a high percentage of patients.

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In recent years several trials demonstrated the efficacy of implantable cardioverter-defibrillator (ICD) therapy for sudden cardiac death prevention and total mortality reduction in particular high-risk groups of patients. The monitoring in the clinical practice of ICD utilization appears very useful in order to follow the application of clinical guidelines and relevant clinical studies.

The Italian ICD Registry was founded in the year 1997 as official member of the

Italian Association of Arrhythmology and Cardiac Pacing (AIAC). The registry collects the data concerning the national activity of ICD implantation based on the official European Registry Implantable Defibrillator (EURID) form. The aim of this review was to report the main epidemiological data and the most important characteristics of patients enrolled in the Italian ICD Registry in the years 2001-2003.

## Methods

ICDs are reported and inserted in the Registry from the ICD implant forms, as communicated after implant procedure. Data are validated for quality of information and uniqueness at data entry and in successive steps at the time of the annual analysis<sup>1-4</sup>.

Data are evaluated according to standard descriptive analyses. Categorical variables are reported in frequencies (%) and absolute numbers, and continuous variables in median (I, III quartile).

## Implantation rate

According to the Registry, the number of ICDs implanted in Italy has been continuing to increase during the last years according to the general trend in European and non-European countries: 2400 in the year 2001, 3934 in the year 2002, and 5318 in the year 2003. The number of ICDs per million of inhabitants in Italy was 42.1 in the year 2001 (+11.8% with respect to 2000), 69.0 in the year 2002 (+63.9% with respect to 2001), 93.3 in the year 2003 (+35.2% with respect to 2002) (Fig. 1). The positive trend of the implantation rate seems to be related to the progressive technological advancement of devices, and to the publication in the same period of important randomized trials showing favorable results in the field of primary and secondary prevention of sudden cardiac death and total mortality reduction such as MUSTT<sup>5</sup>, CASH<sup>6</sup>, CIDS<sup>7</sup>, and MADIT-II<sup>8</sup>. The long-term application in clinical practice of previously published studies, especially MADIT<sup>9</sup> and AVID<sup>10</sup> trials, could have also contributed to the increase in the use of ICDs in our country.

In all the period considered, the Registry obtained the clinical and epidemiological data of about 85% of

all ICD implantation activity in Italy (data from the manufacturers).

The number of centers participating in the Registry increased progressively from 273 in the year 2001 to 304 in 2002, and to 340 in 2003, representing more than 95% of all implanting centers. In the years 2001 and 2002 the majority of implanting centers showed a low-volume activity (1 to 5 ICDs implanted per year), followed by centers with a medium or medium-high volume (6 to 10, and 11 to 20), and finally, by centers with a high-level ICD implantation activity (> 20 devices per year) (Fig. 2). In the year 2003, however, the number of centers with a high-volume activity reached the number of centers with a medium-level activity. Of note, the implantation rate differed markedly in the diverse Italian regions; in Lombardy, for example, the number of ICDs per million of inhabitants was 148.0, in Piedmont 108.7, in Latium 93.9, in Sicily 50.8; the lowest implantation rate occurred in Molise (by 22 per million) (Fig. 3).

## Age and gender

The median age of patients treated with first implantation plus replacement of ICD was 67 years (range 59-73 years) in the year 2001, 67 years (range 59-74 years) in the year 2002, and 68 years (range 58-74 years) in the year 2003<sup>2-4</sup>. The prevalence of male patients was significantly higher in all period considered (79.3% in 2001, 82.3% in 2002, and 81.4% in 2003).

## Symptoms

Figure 4 summarizes the main clinical profile at the moment of ICD implantation. In 2003 the main indication in symptomatic patients was syncope (25.5% of

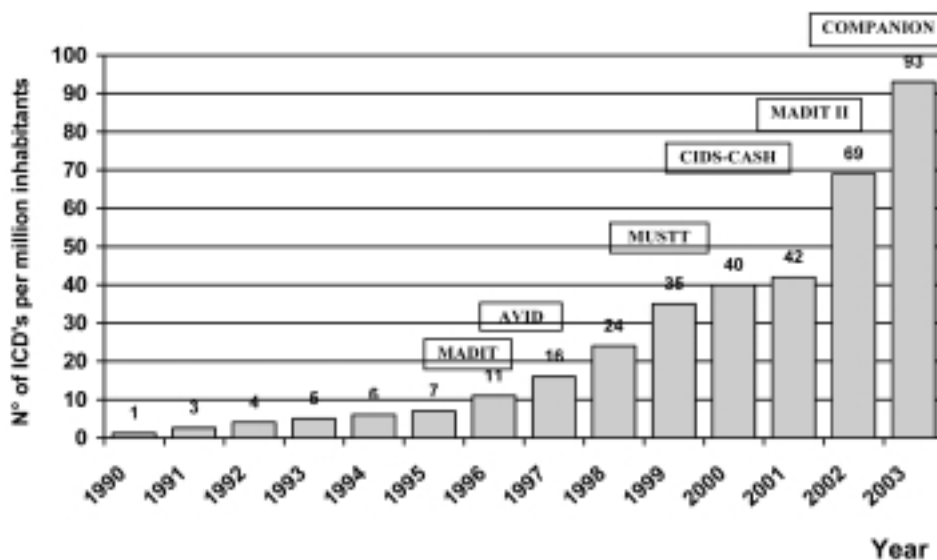


Figure 1. Cardioverter-defibrillator (ICD) implantation rate in Italy.

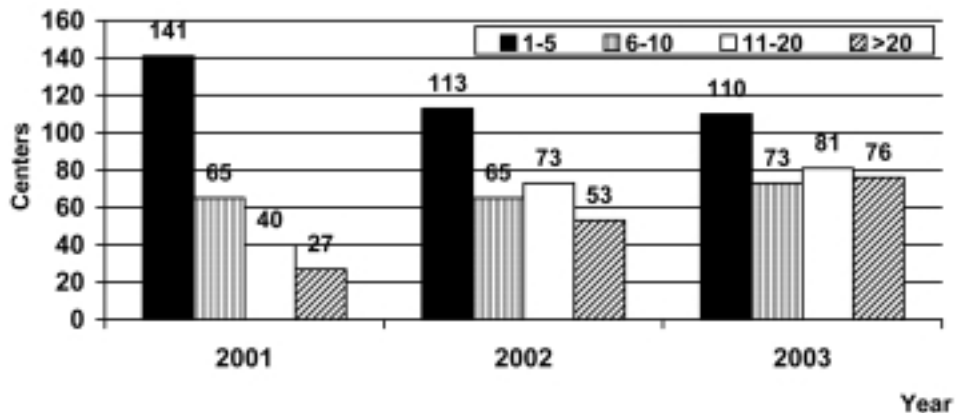


Figure 2. Cardioverter-defibrillator implantations by centers.

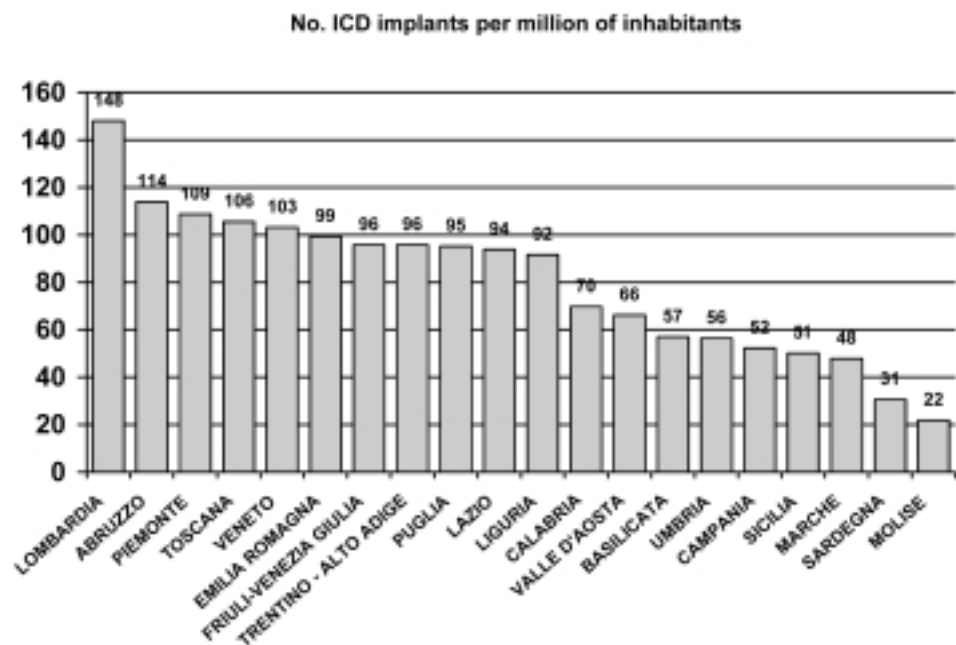


Figure 3. Cardioverter-defibrillator (ICD) implantation rate by regions (year 2003).

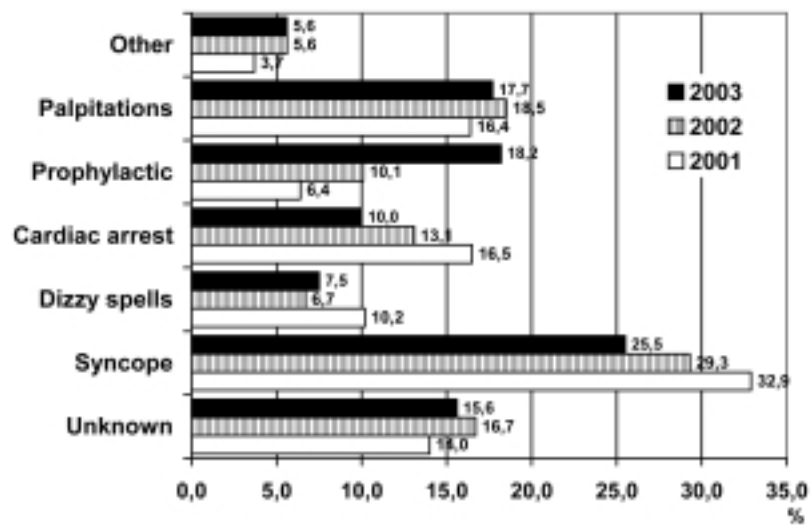


Figure 4. Distribution of cardioverter-defibrillator implantations by symptoms.

any indication for ICD implant), followed by palpitations (17.7%) and cardiac arrest (10.0%), although a relative progressive decline of its rate was evident in the last 3 years. Even the rate of cardiac arrest, the most important clinical indication at the beginning of the ICD era, showed a relative decrease from 16.5% in 2001 to 10.0% in 2003. Palpitations and dizzy spells remained stable, regarding 16.4 to 17.7% and 10.2 to 7.5% of patients, respectively.

The prophylactic use of ICD in patients considered at risk of sudden cardiac death but without history of sustained ventricular tachycardia, had a 3-fold increase during the 3 years, from 6.4% in 2001 to 18.2% in 2003, reflecting the implementation of important randomized studies in the field of primary prevention such as MADIT<sup>9</sup>, MUSTT<sup>5</sup>, MADIT-II<sup>8</sup>, and COMPANION<sup>11</sup>.

### Electrocardiographic indications

Figure 5 indicates the principal arrhythmic indications to ICD therapy. Ventricular tachycardia was considered the index arrhythmia in 50.4 to 55.0% of cases, ventricular fibrillation in 13.5 to 18.1, ventricular fibrillation plus ventricular tachycardia in the same cases in 4.1 to 6.5%. Non-sustained ventricular arrhythmias were reported in 5.2 to 15.1% of patients. Of note, the discrepancy between the lower rate of cardiac arrest as clinical indication (see above) in comparison to the higher rate of ventricular fibrillation and ventricular fibrillation plus ventricular tachycardia as ECG indication, was probably related to the different definition of accompanying symptoms in some centers.

### Etiology

In the period 2001-2003 the prevalent underlying heart disease was represented by coronary artery dis-

ease; the different typology of vessel disease in patients with or without previous myocardial infarction is indicated in table I. In the same period, non-ischemic dilated cardiomyopathy was reported in 21.3 to 22.6% of cases, hypertrophic cardiomyopathy in 3.0 to 3.8%, arrhythmogenic right ventricular cardiomyopathy/dysplasia in 1.5 to 1.9%, valvular heart disease in 1.4 to 1.8%, long QT syndrome in 0.5 to 0.7%, and finally, idiopathic life-threatening ventricular tachyarrhythmias in 1.6 to 1.9% of patients (Table I). The typology of heart disease appears similar considering the group of patients treated with an ICD for primary prevention of sudden death with respect to the group of all ICD recipients (Table II).

### Functional class and left ventricular function

In all series NYHA class II and III are prevalent, ranging from 29.4 to 38.4% and from 19.9 to 26.9%, respectively (Fig. 6). The percentage of patients in NYHA class I diminished progressively in the period 2001-2003 (15.5 to 10.1%), while the number of patients in NYHA class IV remained stable and very low (2.0 to 1.9%), probably representing a group of patients treated with an ICD only as a bridge to heart transplantation. In a not negligible percentage of cases the functional class was unavailable due to the clinical difficulty to classify correctly some patients at the moment of ICD implantation.

Left ventricular ejection fraction was not reported as a continuous variable but was divided into three main subgroups (> 50%, between 30 and 50%, < 30%) according to the EURID form. During the 3 years, the vast majority of patients presented at the enrollment either a mildly or severe reduction in ejection fraction (30 to 50%, < 30%), followed by the group of patients with good left ventricular function (> 50%) (Fig. 7). A subanalysis of the main symptom indications did not

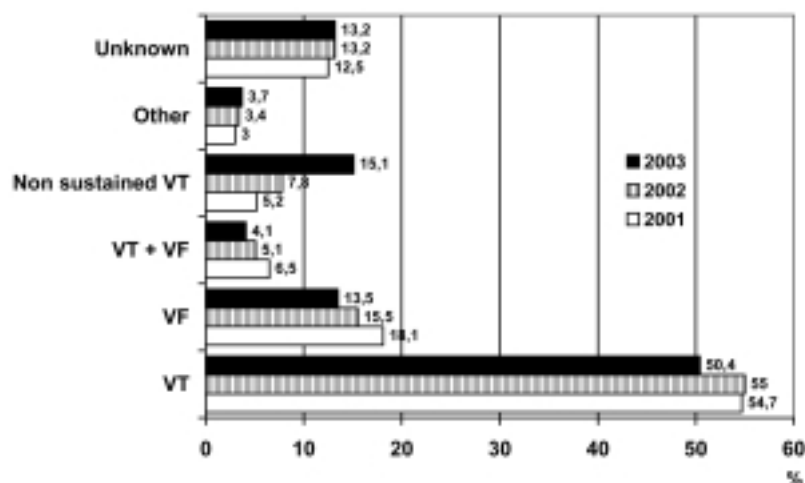


Figure 5. Distribution of cardioverter-defibrillator implantations by ECG indications. VF = ventricular fibrillation; VT = ventricular tachycardia.

**Table I.** Distribution of cardioverter-defibrillator implantations by etiology.

	2001 (n=2400)	2002 (n=3934)	2003 (n=5318)	Combined (n=11 652)
Unknown	475 (19.8%)	771 (19.6%)	871 (16.4%)	2117 (18.2%)
Post-myocardial infarction				
1-vessel CAD	359 (14.9%)	414 (10.5%)	567 (10.7%)	1340 (11.5%)
2-vessel CAD	138 (5.8%)	209 (5.3%)	300 (5.6%)	647 (5.6%)
3-vessel CAD	130 (5.4%)	231 (5.9%)	295 (5.5%)	656 (5.6%)
Coronary anatomy unknown	300 (12.5%)	653 (16.6%)	1175 (22.1%)	2128 (18.3%)
Post-multiple myocardial infarction				
1-vessel CAD	14 (0.6%)	13 (0.3%)	12 (0.2%)	39 (0.3%)
2-vessel CAD	16 (0.7%)	25 (0.6%)	25 (0.5%)	66 (0.6%)
3-vessel CAD	2 (0.1%)	33 (0.8%)	40 (0.8%)	75 (0.6%)
Coronary anatomy unknown	–	36 (0.9%)	58 (1.1%)	94 (0.8%)
No myocardial infarction				
1-vessel CAD	12 (0.5%)	11 (0.3%)	13 (0.2%)	36 (0.3%)
2-vessel CAD	10 (0.4%)	10 (0.3%)	6 (0.1%)	26 (0.2%)
3-vessel CAD	9 (0.4%)	7 (0.2%)	18 (0.3%)	34 (0.3%)
Coronary anatomy unknown	7 (0.3%)	20 (0.5%)	22 (0.4%)	49 (0.4%)
Valvular heart disease	43 (1.8%)	56 (1.4%)	95 (1.8%)	194 (1.7%)
Dilated cardiomyopathy	541 (22.6%)	881 (22.4%)	1132 (21.3%)	2554 (21.9%)
Hypertrophic obstructive cardiomyopathy	91 (3.8%)	144 (3.7%)	159 (3.0%)	394 (3.4%)
ARVD/cardiomyopathy	45 (1.9%)	65 (1.7%)	79 (1.5%)	189 (1.6%)
Other cardiomyopathies	69 (2.9%)	133 (3.4%)	148 (2.8%)	350 (3.0%)
Idiopathic	45 (1.9%)	64 (1.6%)	83 (1.6%)	192 (1.6%)
Long QT syndrome	13 (0.5%)	27 (0.7%)	35 (0.7%)	75 (0.6%)
Other	81 (3.4%)	131 (3.4%)	185 (3.5%)	397 (3.4%)

ARVD = arrhythmogenic right ventricular dysplasia; CAD = coronary artery disease.

**Table II.** Distribution of cardioverter-defibrillator implantations by etiology in primary prevention (prophylactic cardioverter-defibrillator implantation).

	2001 (n=154)	2002 (n=398)	2003 (n=967)	Combined (n=1519)
Unknown	15 (9.7%)	22 (5.5%)	50 (5.2%)	87 (5.7%)
Post-myocardial infarction				
1-vessel CAD	19 (12.3%)	43 (10.8%)	140 (14.5%)	202 (13.3%)
2-vessel CAD	12 (7.8%)	26 (6.5%)	58 (6.0%)	96 (6.3%)
3-vessel CAD	10 (6.5%)	31 (7.8%)	89 (9.2%)	130 (8.6%)
Coronary anatomy unknown	14 (9.1%)	75 (18.8%)	211 (21.8%)	300 (19.7%)
Post-multiple myocardial infarction				
1-vessel CAD	–	2 (0.5%)	4 (0.4%)	6 (0.4%)
2-vessel CAD	3 (1.9%)	7 (1.8%)	6 (0.6%)	16 (1.1%)
3-vessel CAD	–	5 (1.3%)	17 (1.8%)	22 (1.4%)
Coronary anatomy unknown	–	6 (1.5%)	20 (2.1%)	26 (1.7%)
No myocardial infarction				
1-vessel CAD	2 (1.3%)	2 (0.5%)	4 (0.4%)	8 (0.5%)
2-vessel CAD	1 (0.6%)	1 (0.3%)	2 (0.2%)	4 (0.3%)
3-vessel CAD	2 (1.3%)	3 (0.8%)	2 (0.2%)	7 (0.5%)
Valvular heart disease	2 (1.3%)	3 (0.8%)	15 (1.6%)	20 (1.3%)
Dilated cardiomyopathy	34 (22.1%)	113 (28.4%)	232 (24.0%)	379 (25.0%)
Hypertrophic obstructive cardiomyopathy	14 (9.1%)	13 (3.3%)	26 (2.7%)	53 (3.5%)
ARVD/cardiomyopathy	4 (2.6%)	6 (1.5%)	9 (0.9%)	19 (1.3%)
Other cardiomyopathies	1 (0.6%)	9 (2.3%)	11 (1.1%)	21 (1.4%)
Idiopathic	3 (1.9%)	8 (2.0%)	21 (2.2%)	32 (2.1%)
Long QT syndrome	4 (2.6%)	2 (0.5%)	3 (0.3%)	9 (0.6%)
Other	14 (9.1%)	21 (5.3%)	47 (4.8%)	82 (5.4%)

ARVD = arrhythmogenic right ventricular dysplasia; CAD = coronary artery disease.

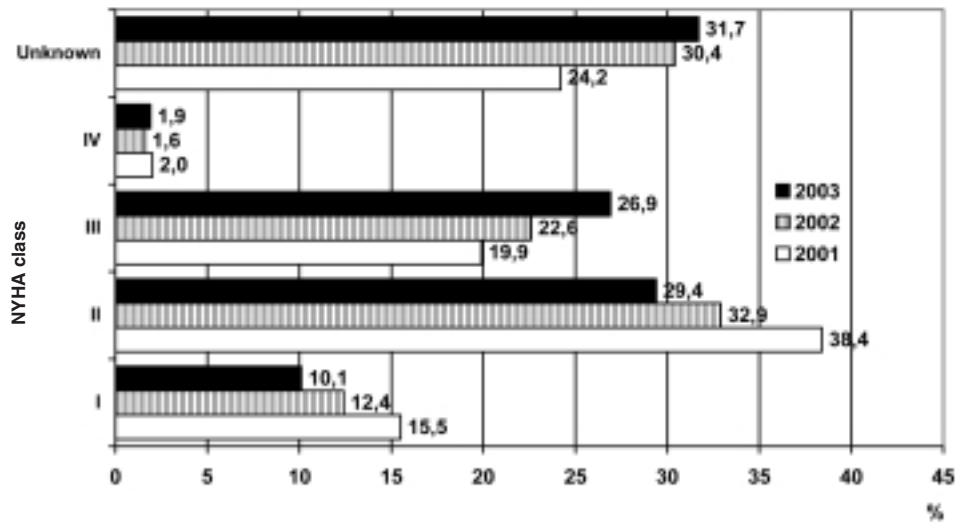


Figure 6. Distribution of cardioverter-defibrillator implantations by the patient's NYHA class.

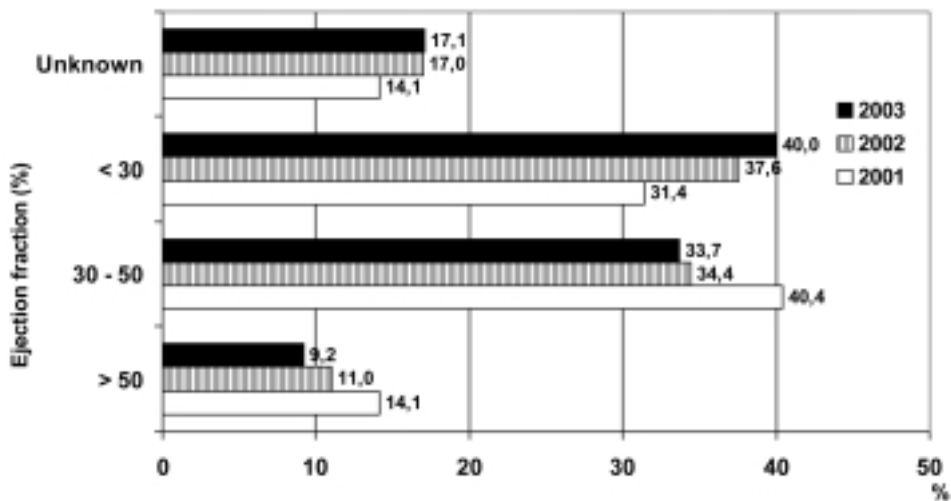


Figure 7. Distribution of cardioverter-defibrillator implantations by the patient's ejection fraction.

reveal particular differences in the four NYHA classes, while a higher prevalence of cardiac arrest and syncope was evident in patients with ejection fraction > 50% compared with patients with ejection fraction < 30% (Tables III and IV). Moreover, the indication to

prophylactic ICD implantation was more frequent in patients with a severe reduction in left ventricular function according to inclusion criteria of the main primary prevention trials evaluating ICD therapy<sup>4,7,8,10</sup>.

Table III. Distribution of cardioverter-defibrillator implantations by NYHA class and symptoms for the period 2001-2003.

	Class I (n=1397)	Class II (n=3780)	Class III (n=2797)	Class IV (n=213)	Unknown (n=3464)	Combined (n=11 651)
Syncope	467 (33.4%)	1157 (30.6%)	720 (25.7%)	41 (19.2%)	911 (28.1%)	3296 (28.3%)
Dizzy spells	93 (6.7%)	397 (10.5%)	265 (9.5%)	17 (8.0%)	135 (3.8%)	907 (7.8%)
Cardiac arrest	246 (17.6%)	490 (13.0%)	295 (10.5%)	34 (16.0%)	375 (10.8%)	1440 (12.4%)
Prophylactic	194 (13.9%)	451 (11.9%)	525 (18.8%)	36 (16.9%)	313 (9.6%)	1519 (13.0%)
Palpitation	238 (17.0%)	768 (20.3%)	521 (18.6%)	32 (15.0%)	500 (16.5%)	2059 (17.7%)
Other	53 (3.8%)	178 (4.7%)	207 (7.4%)	25 (11.7%)	141 (4.5%)	604 (5.2%)
Unknown	106 (7.6%)	339 (9.0%)	264 (9.4%)	28 (13.1%)	1089 (26.8%)	1826 (15.7%)



**Table IV.** Distribution of cardioverter-defibrillator implantations by ejection fraction and symptoms for the period 2001-2003.

	> 50% (n=1262)	30-50% (n=4113)	< 30% (n=4358)	Unknown (n=1918)	Combined (n=11 651)
Syncope	474 (37.6%)	1317 (32.0%)	1105 (25.4%)	400 (25.8%)	3296 (28.3%)
Dizzy spells	79 (6.3%)	393 (9.6%)	358 (8.2%)	77 (3.6%)	907 (7.8%)
Cardiac arrest	237 (18.8%)	556 (13.5%)	509 (11.7%)	138 (7.8%)	1440 (12.4%)
Prophylactic	154 (12.2%)	420 (10.2%)	831 (19.1%)	114 (6.2%)	1519 (13.0%)
Palpitation	190 (15.1%)	839 (20.4%)	774 (17.8%)	256 (17.0%)	2059 (17.7%)
Other	44 (3.5%)	171 (4.2%)	312 (7.2%)	77 (3.6%)	604 (5.2%)
Unknown	84 (6.7%)	417 (10.1%)	469 (10.8%)	856 (36.0%)	1826 (15.7%)

**Antiarrhythmic drugs and previous cardiac intervention**

Antiarrhythmics were frequently used when the physicians decided to treat the patient with an ICD. In particular, at the moment of ICD implantation, amiodarone therapy was administered alone or plus other antiarrhythmics in 29.7 to 40.0% of patients (Fig. 8). Data concerning the persistent use or discontinuation of antiarrhythmic drugs after ICD treatment are not available.

Coronary artery bypass graft was previously performed in 10.6 to 11.3% of cases, while left ventricular aneurysmectomy and transcatheter radiofrequency ablation in only a very low percentage of patients (Fig. 9).

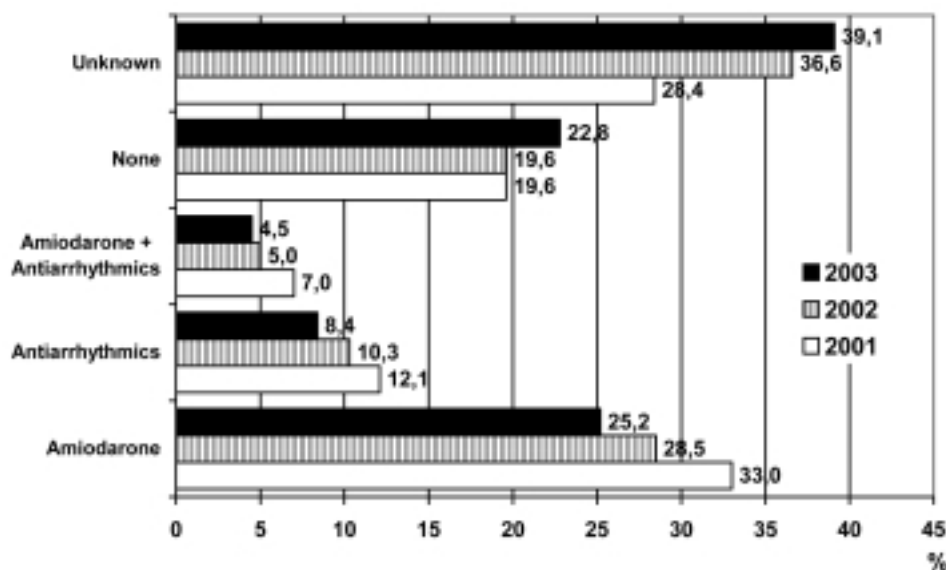
**Typology of implantable cardioverter-defibrillator**

The selection of ICD type was correctly obtained only for the years 2002 and 2003. Single-chamber ICDs were chosen in 45.7 and 39.2% of patients, dual-

chamber ICDs in 34.9 and 32.4%, and biventricular ICDs in 19.4 and 28.4% (Fig. 10). The high utilization rate in Italy of ICD with cardiac resynchronization therapy could be related to the favorable results obtained in some trials such as COMPANION<sup>11</sup> and MIRACLE<sup>12</sup>, and to the strict cooperation between heart failure clinics and electrophysiologic laboratories.

**Conclusion**

The ICD implantation rate in Italy increased significantly in the last 3 years, similarly to the trend in other western countries and following the publication of controlled studies in the field of primary and secondary prevention of sudden cardiac death. In particular, the number of ICDs per million of inhabitants increased from 69 in the year 2002 to 94 in the year 2003. Moreover, the Italian ICD Registry showed during the last 3 years an important increase in prophylactic ICD utilization (accounting for 18.2% of the total implantation rate in 2003). Among the published randomized trials,



**Figure 8.** Distribution of cardioverter-defibrillator implantations by drugs at implant.

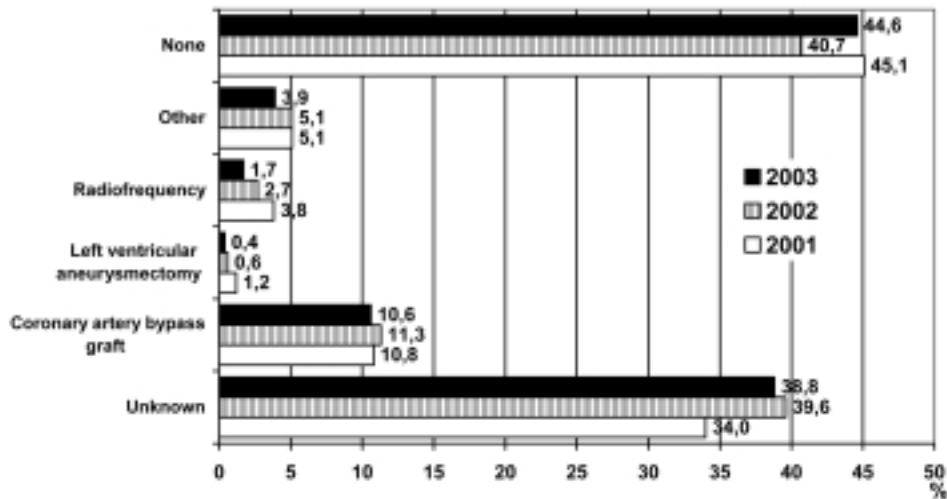


Figure 9. Distribution of cardioverter-defibrillator implantations by type of previous cardiac intervention.

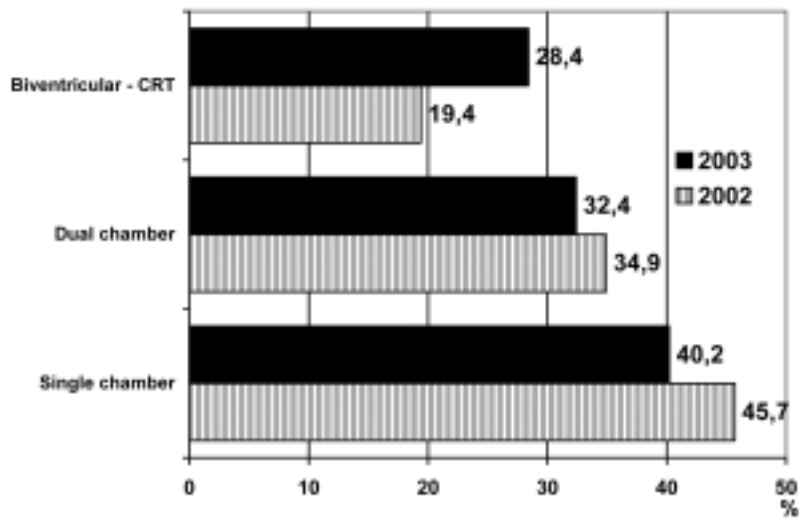


Figure 10. Distribution of implantations by cardioverter-defibrillator type. CRT = cardiac resynchronization therapy.

MADIT-II results had a major clinical impact on the Italian community of cardiologists/electrophysiologists.

A sophisticated ICD, including dual-chamber pacing or cardiac resynchronization therapy, was chosen in a higher percentage of patients (32.4 and 28.4% of all implantation rates in 2003, respectively), probably due to the poor clinical characteristics of the patients enrolled and to the preliminary presentation of the COMPANION trial results.

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